

American Journal of Obstetrics and Gynecology

VOL. 63

MARCH, 1952

No. 3

*Transactions of the American Association of Obstetricians,
Gynecologists and Abdominal Surgeons
Sixty-Second Annual Meeting
Hot Springs, Va., Sept. 6, 7, and 8, 1951*

(Continued from the February issue)

VESICOVAGINAL FISTULAS*

BAYARD CARTER, M.D., LEONARD PALUMBO, M.D., ROBERT N. CREADICK, M.D.,
AND ROBERT A. ROSS, M.D., DURHAM, N. C.

*(From the Department of Obstetrics, Gynecology, and Endocrinology, Duke University
School of Medicine)*

WE REPORT our experiences and results, during recent years, with patients who had operations for the cure of vesicovaginal fistulas.

This study covers the last 175 months and consists of a small series of 73 consecutive patients admitted and operated upon for various types of urinary fistulas. Fistulas other than vesicovaginal are included to illustrate the contrasts in results for the various types of fistulas. Ureterovaginal fistulas, however, are not included.

In this series of 73 patients, there were 57 (78.1 per cent) vesicovaginal, 8 (11 per cent) urethrovesicovaginal, 3 (4.1 per cent) urethrovaginal, and 5 (6.8 per cent) vesicocervicovaginal fistulas.

The series is small. We have noted that the number of patients admitted to our clinic with urinary and bowel fistulas has steadily decreased during recent years. In the last five years of this report, we have admitted but 4 patients with urinary fistulas due to obstetric trauma, 18 due to gynecologic operative trauma, 4 due to irradiation therapy for cancer of the cervix, and 2 due to

*Presented at the Sixty-second Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 6, 7, and 8, 1951.

NOTE: The Editors accept no responsibility for the views and statements of authors as published in their "Original Communications."

irradiation therapy followed by some type of abdominal hysterectomy for cancer of the cervix. In the last five years, therefore, we have admitted but 28 patients with fistulas of the urinary tract. This decrease in the number of fistulas in comparison to the increased number of gynecologic admissions is a serious problem when house staff training is considered. It is necessary to have a variety of fistulas to insure experience in this important part of gynecologic technique.

The operations on these 73 patients were done by five members of the upper staff and by eighteen members of the house staff. The series, therefore, in no way represents the results of one or two selected gynecologists.

Literature

A review of the literature on vesicovaginal fistula is not necessary. The historical facts have been adequately presented in Mahfouz Bey's¹³ and Miller's²¹ complete and stimulating reviews.

Some of the significant papers¹⁻¹⁹ which appeared following Sims'¹ article and up to 1935 are listed. We have tabulated also some of the more important publications²⁰⁻⁶⁶ from 1935 to 1950. Table I presents representative series in these two eras and permits certain comparisons.

Kelly⁷ listed the various operative approaches for closure of these fistulas. Briefly, these approaches include the parasacral, ischiorectal, transperitoneal,

TABLE I

NAME	YEAR	NO. OF PA- TIENTS	ROUTE	CURES	PER CENT CURED	MOR- TALITY PER CENT
1. Sims ^{*1}	1860	261	Vaginal	216	82.7	
2. Simon [*]	1869	105	Vaginal	92	89.5	
3. Legueu [*]	1928	24	Transvesical		64.0	
			Transabdominal		89.0	
4. Judd ⁹	1920	56	Vaginal chiefly	42	82.0	
5. Sears ¹²	1929	50	Transvesical	40	80.0	6
		(col- lected)				
6. Mahfouz Bey ¹³	1930	300	Vaginal chiefly		87.0	
		100	Vaginal chiefly		95.0	
7. Apajalahti ¹⁴	1931	159	Vaginal chiefly	118	74.0	
8. Rawls [*]	1934	23	Vaginal	21	91.3	
9. Schmitz ²⁰	1935	17	Vaginal (95%)	17	100.0	0
10. Pemberton and Smith ²³	1936	100	Vaginal chiefly	84	84.	2
11. Counseller ²⁵	1937	181	Vaginal chiefly			
12. Franche ²⁷	1938	24	Vaginal	21	87.5	
		50	Transvesical	48	96.0	
13. Masson and Wilson ³⁴	1941	48	Vaginal (85%)	42	87.5	4.2
14. Miller, N. ³⁸	1942	51	Vaginal (100%)	43	85.0	0
15. Latzko ³⁷	1942	31	Vaginal (Latzko Type)	29	93.5	0
16. Roberts ⁴² (Obst. vesicovaginal fistula)	1944	90	Ureteral transplantation			14.4
17. Hayes ⁴⁷	1945	85	Vaginal chiefly	73	86.0	2.3
18. Aldridge ⁴⁹	1946	75	Vaginal chiefly	60	80.0	5.3
19. Te Linde ⁵³	1947	41	Vaginal	37	90.2	0
20. Harguindey ⁶²	1949	100	Vaginal	91	91.0	
21. Krishnan ⁵⁶	1949	100	Vaginal chiefly	87	87.0	1
22. Phaneuf ⁵⁷	1949	40	All types including ure- teral transplantation	39	97.5	0
23. Tyrone ⁶⁰	1949	33	Vaginal (1 ureteral transplantation)	32	97.0	
24. Bramhall ⁶⁶	1950	13	Transvesical	12	92.3	* 7.7

*Quoted from Miller.²¹

paravaginal, vaginal, transvulval, transurethral, vestibular, transpubic, trans-symphyseal, suprapubic extraperitoneal, and transvesical-transabdominal routes.

Miller²¹ states that only the vaginal, the suprapubic-transvesical, and the transabdominal operations are "sound and practicable." He emphasizes that the suprapubic-transvesical operation ranks second to the vaginal procedure.

Sears¹² selected fifty patients who had the transvesical operation with an 80 per cent cure rate and a mortality of 6 per cent. Bramhall⁶⁶ did the transvesical operation in thirteen patients and had a 92.3 per cent cure rate but a mortality rate of 7.7 per cent.

Colpocleisis has found few advocates in recent years. Latzko³⁷ has had excellent results with his obliteration operation. It should be noted that he advised this procedure only for patients whose uteri had been removed.

Ureteral transplantation, which has been done for various types of urinary fistulas, has been featured by a high mortality rate. Roberts⁴² reported ninety operations with a mortality rate of 14.4 per cent and Thompson⁴⁵ reported thirteen operations with a mortality rate of 38.6 per cent. Counseller²⁵ states that ureterosigmoidal anastomosis is indicated when there is complete absence of the vesical sphincter or when the bladder is severely contracted.

After a review of the literature it is apparent that the vaginal operation is still the method of choice. It is also evident that there has been the general tendency to substitute catgut sutures for silver wire and other metallic suture material.

It is difficult to interpret and to compare many of the reported series of fistulas. There is a real need for standard methods to describe the fistulas, the actual operations, and results. We believe there should be stated: (1) The etiology and duration of the fistula; (2) its location, size, and type; (3) its accurate description by complete and competent urologic survey; (4) accurate anatomic statements of what tissues are involved; (5) a concise and definite statement of the operation done; (6) results in terms of "cure" or "failure."

Material

Table II gives the general outline for the 73 consecutive fistulas upon which this study is based. Obstetric injury was responsible for 38.4 per cent of the fistulas; gynecologic injury for 59 per cent; and injury, not due to obstetric or gynecologic trauma, was responsible for 2.8 per cent.

TABLE II. SEVENTY-THREE CONSECUTIVE FISTULAS

	TOTAL FIS- TULAS		VESICO- VAGINAL		URE- THRO- VESICO- VAGINAL		URE- THRO- VAGINAL		VESICO- CERVICO- VAGINAL		OPERA- TIVE CURES		OPERA- TIVE FAIL- URES	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Obstetric (all follow- ing vaginal de- liveries)	28	38.4	15	53.6	7	25	2	7.1	4	14.3	24	86	4	14.3
Gynecologic	43	59	40	93	1	2.3	1	2.3	1	2.3	37	86	6	14
Traumatic (nonopera- tive)	1	1.4	1	100	0		0		0		1	100	0	
Neurogenic	1	1.4	1	100	0		0		0		1	100	0	
Total	73	100	57	78.1	8	11	3	4.1	5	6.8	63	86.3	10	13.7

Table III presents data on the 28 obstetric fistulas and for the two fistulas due to trauma not of obstetric or gynecologic origin.

Table IV concerns the 43 fistulas due to various gynecologic injuries.

TABLE III. OBSTETRIC FISTULAS (28)

	TOTAL FISTULAS		VESICO-VAGINAL		URETHRO-VESICO-VAGINAL		URETHRO-VAGINAL		VESICO-CERVICO-VAGINAL		OPERATIVE CURES		OPERATIVE FAILURES	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Vaginal delivery	28	100	15		7		2		4		24	85.8	4	14.3
					(2 Failed)				(2 Failed)					
Abdominal delivery	0		0		0		0		0		0		0	
Total	28		15	53.6	7	25	2	7.1	4	14.3	24	85.8	4	14.3
FISTULAS OTHER CAUSES (2)														
Traumatic (nonoperative)	1		1		0		0		0		1		0	
Neurogenic	1		1		0		0		0		1		0	
Total	2	100	2		0		0		0		2	100	0	

TABLE IV. GYNECOLOGIC FISTULAS (43)

CAUSE OF FISTULAS	TOTAL FISTULAS		VESICO-VAGINAL	URETHRO-VESICO-VAGINAL	URETHRO-VAGINAL	VESICO-CERVICO-VAGINAL	OPERATIVE CURES		OPERATIVE FAILURES	
	NO.	%					NO.	%	NO.	%
Abdominal operations	26	60.5	26 (1 Failed)	0	0	0	25	96.2	1	3.9
Vaginal operations	5	11.6	3	1	1	0	5	100	0	
Irradiation:										
Malignant	8	18.6	7 (1 Failed)	0	0	1 (1 Failed)	6	75	2	25
Nonmalignant	1	2.3	1 (1 Failed)	0	0	0	0		1	100
Irradiation and operation:										
Malignant	3	7	3 (2 Failed)	0	0	0	1	33.3	2	66.7
Nonmalignant	0		0	0	0	0	0		0	
Total	43		40	1	1	1	37	86	6	14

General Data

*Obstetric Fistulas (28).—**Duration of 16 fistulas present for 1 year or longer:**Years:* 11, 6, 5, 1 plus, 10, 22, 3, 28, 12, 21, 15, 2, 17, 1 plus, 21, 1 plus.

Three failures (18.7 per cent) occurred in patients with fistulas present 5, 28, and 21 years.

*Duration of 12 fistulas present for less than 1 year:**Months:* 4, 4, 3 plus, 5, 2, 5, 6, 4, 3, 6, 9, and 4.

One failure (8.3 per cent) occurred in one patient with a fistula of 5 months' duration.

White patient totaled 15; Negro patients, 13; rural patients totaled 22, city or town patients, 6. The oldest patient was 56 years of age whereas the youngest was 14. Seven Negro patients and one white patient had syphilis (35.7 per cent). Two (15.38 per cent) of the Negro patients had diabetes mellitus. The lowest parity in the group was i-0-i; the highest parity was xii-0-vii. These occurred in white patients.

It was noted on review of the histories that there were delivered, at the time the fistulas were caused, 9 stillborn infants (60 per cent) in the 15 white patients and 10 stillborn infants (76.9 per cent) in the 13 Negro patients. One Negro infant, by history, was delivered by a destructive operation.

Two of the patients in this group had drug addiction. It was impossible to determine with accuracy how many more were addicted.

According to the histories only 5 patients became pregnant after the fistulas occurred and delivered while the fistulas were draining. Nineteen of the 28 patients were of childbearing age.

Six patients had absence of uterine bleeding after the fistulas appeared for 5, 6, 8, 24, 12, and 20 months. We thought that more patients in this obstetric group would have infrequent and scanty, or even cessation of, uterine bleeding. This thought was not substantiated. One patient, aged 49 years, had no uterine bleeding for two years prior to the repair of the fistula. After the repair, she began normal, cyclic, uterine bleeding and continued to bleed cyclically for one and one-half years. A second patient, aged 47 years, had but one or two episodes of scanty uterine bleeding during the 17 years in which her fistula drained. One month after repair, she started cyclic uterine bleeding which continued for two years. A third patient, aged 31 years, had no uterine bleeding for the 20 months during which her fistula drained. Following repair of the fistula, she resumed normal cyclic bleeding.

It would be interesting to have the opportunity to study the bleeding histories of a large series of women of childbearing age who have draining fistulas, and to study the endometrial patterns in those patients who have infrequent, scanty, or no uterine bleeding. An investigation of the psychosomatic influences exerted on the bleeding by the constant drainage of urine would also be worth while. The study by psychosomatic methods of those patients who permit fistulas to drain for so long a time would also be interesting.

Gynecologic Fistulas (43).—Twenty-six fistulas in this group followed abdominal operations and 5 followed vaginal operations:

Duration of 12 fistulas present for one year or more.

Years: 1 plus, 10, 10, 2, 3, 17, 7, 7, 7, 7, 1 and 2 plus.

No failures in repair occurred in these 12 patients.

Duration of 19 fistulas for less than 1 year.

Months: 7, 9, 9, 7, 9, 6, 8, 8, 4 plus, 6 plus, 5, 6, 7, 7, 7, 3, 7, 8, 3 plus.

One failure in repair occurred in a patient with a vesicovaginal fistula produced by abdominal operation 5 months before attempted repair.

Nine fistulas followed irradiation therapy:

Duration of 8 fistulas present for one year or more.

Years: 1 plus, 1 plus, 1 plus, 1 plus, 3 plus, 4, 5, 6 plus.

Two failures occurred in fistulas present for 4 years and for 1 plus years.

Both were vesicovaginal fistulas.

Duration of one fistula present for less than 1 year.

Months: 6

Failure occurred in this patient with a vesicovaginal fistula caused by irradiation for squamous-cell carcinoma of the cervical stump.

Three fistulas followed irradiation and operation for cancer of the cervix uteri:

Duration of 1 fistula was 14 years.

Operation was a failure in vesicovaginal and rectovaginal fistula repair.

Duration of 2 vesicovaginal fistulas in months.

Months: 3, 5

One operation failed in a patient with diabetes mellitus and fistula present for 5 months.

Two fistulas due to other causes:

1. *Trauma by Foreign Body.*—This was a vesicovaginal fistula in a 12-year-old, white, single, rural, para 0-0-0. She had fallen on a cornstalk which had perforated the rectum and bladder four months prior to admission to the clinic. The perforation of the bowel had healed but the vesicovaginal fistula persisted. She had been in a hospital in a neighboring city for three months but no operative attempt had been made to close the fistula. The patient was found to have many fragments of cornstalk encrusted with salts in the bladder. Suprapubic cystolithotomy, with removal of the foreign bodies, and repair of fistula were done with success.

2. *Trauma to Spinal Cord With Paraplegia.*—This was a vesicovaginal fistula in a 35-year-old, white, urban, para ii-0-ii. She injured her back in an accident fourteen years

previously and was paralyzed from the waist down. She was diagnosed as a "paraplegic." In 1930 in a medical center in a near-by state a spinal fusion operation was performed. She was unable to void for two months after this procedure and had to be catheterized. She gradually had return of some sensory and motor power. She never had complete control of voiding and leaked through the urethra. In 1932 she had, in a near-by city, a suspension of the uterus with ligation of tubes and removal of the appendix. Six months after this operation urinary leakage developed. The patient was told she had a vesicovaginal fistula. She demanded attempted repair of the fistula although it was explained to her that even if the fistula were closed she would still have hyperdistention of the bladder. In 1939 by vaginal operation and use of chromic catgut sutures the vesicovaginal fistula was repaired. It held for 20 days and then broke down. Five months later another vaginal repair with chromic catgut sutures was done and was successful. In 1946 she again came to the clinic with a report that she had had no vaginal leakage of urine for over six years, but that in the past week she had leaked. It could not be determined whether this was a recurrence of the old, or a new vesicovaginal fistula. The fistula was repaired by vaginal operation with chromic catgut sutures and has not leaked since 1946. She has been emptying the bladder satisfactorily with the aid of suprapubic pressure.

In these 43 patients with fistulas caused by gynecologic procedures and in the 2 patients with fistulas caused by trauma: 32 were white, 1 was an Indian and 12 were Negroes; rural patients totaled 29; city or town patients, 16; the oldest patient was 73 years of age, the youngest, 12. Two Negro, 1 white, and 1 Indian patient had syphilis (8.8 per cent). One Negro patient also had lymphopathia venereum. Two white patients and 1 Negro patient had diabetes mellitus (6.6 per cent). The highest parity in the group was that of a white patient, para xii-ii-vii; 8 patients had never been pregnant. All but 2 patients were married. Two of the patients had severe drug addiction. It was impossible to determine with any accuracy how many more of the patients were addicted.

Preoperative Care

There were no original features in preoperative care. There was one rule, however, which had to be followed in all patients. This was that full urologic studies of urethra, bladder, ureters, and kidneys were mandatory. This necessary part of the work-up of these patients is one of the best ways to have house officers comprehend the problems which these patients present.

The general health of the patient and the necessity for improving the nutritional and hematologic status were the next most important features of preoperative care.

Attempts to improve the condition of the actual operative field were less well standardized. Some surgeons ordered sitz baths, douches, and hormone therapy in the preoperative period; others did not. Practically all operators made a serious effort to cure urinary infection prior to operation. The use of chemotherapeutic and antibiotic agents was common. Opinions varied concerning how and when to acidify the urine. In the majority of instances the urine was acidified for three to five days prior to operation.

In the more complicated types of fistulas ureteral catheters were inserted before the operation was started.

Emphasis was placed upon those fistulas produced by irradiation therapy or by irradiation therapy followed by operation. It is in this group that the majority of failures occurred. The necessity for maintenance of vaginal and cervical patency in the management of patients with carcinoma of the cervix is best stressed when these irradiated patients present themselves with the marked fibrotic changes and the distorted vaginas caused by the therapy.

The psychosomatic problems of many of these patients also demanded intelligent and sympathetic interest. Many showed depressive features. Others had drug addiction of minor and major degrees.

Operations

Table V is an analysis of the operations.

Forty-two of the 73 patients had had no operations for closure of the fistulas before entering the clinic. Thirty-one patients had had 62 unsuccessful operations prior to admission.

TABLE V. ANALYSIS OF OPERATIONS

CAUSE OF FISTULAS	NO PREVIOUS OPERATIONS	OPERATIONS ELSEWHERE		OPERATIONS AT CLINIC		TOTAL	
	PA-TIENTS	PA-TIENTS	OPERA-TIONS	PA-TIENTS	OPERA-TIONS	PA-TIENTS	OPERA-TIONS
Obstetric (all following vaginal delivery)	14	14	30	28	42	28	72
Gynecologic	26	17	32	43	51	43	83
Abdominal operations	14	12	24	26	30		
Vaginal operations	3	2	2	5	6	26	54
Irradiation	7	2	5	9	11	5	8
Irradiation and operation	2	1	1	3	4	9	16
Traumatic	1	0	0	1	1	3	5
Neurologic	1	0	0	1	3	1	1
Total	42	31	62	73	97	1	3
						73	159

In the clinic, 73 patients had a total of 97 operations for cure in 63 patients and for failure of cure in 10 patients as shown in Table VI.

TABLE VI. OPERATIVE RESULTS—73 PATIENTS, 97 OPERATIONS

RESULT	ONE ATTEMPT	TWO ATTEMPTS	THREE ATTEMPTS	PATIENTS	OPERATIONS
Cure	48, or 76.2%	11, or 17.5%	4, or 6.3%	63	82
Failure	7	1	2	10	15
Total	55	12	6	73	97

In summary, then, either elsewhere or in this clinic, 159 operations were performed.

In the clinic all but two of the operative attempts for closure were made by vaginal operations. One patient had a suprapubic cystolithotomy with removal of foreign bodies from the bladder and had successful closure of a vesicovaginal fistula. Another patient, who had a vesicovaginal fistula caused by irradiation therapy followed by abdominal hysterectomy in the treatment of squamous-cell carcinoma of the cervix, had a successful suprapubic closure of the fistula.

There were successful closures made in 17 consecutive fistulas and this was the greatest number of successful closures in sequence in the entire series of 73 fistulas. The fistulas in this series of 17 were three vesicovaginal, two vesicocervicovaginal, and one urethrovesicovaginal, all six of which were caused by obstetric trauma. The remaining 11 fistulas were 8 vesicovaginal and one urethrovesicovaginal which followed abdominal hysterectomy; one vesicovaginal which followed an attempt elsewhere to do vaginal hysterectomy, and one vesicovaginal which occurred after radium and x-ray therapy for squamous-cell carcinoma of the cervix.

TABLE VII. FAILURES—CAUSE AND LOCATION

CAUSE OF FISTULA	TYPE OF FISTULA										TOTAL	
	VESICOVAGINAL		URETHROVESICO-VAGINAL		URETHRO-VAGINAL		VESICOCERVICO-VAGINAL					
	NO.	FAILURES	NO.	FAILURES	NO.	FAILURES	NO.	FAILURES	NO.	FAILURES		
Obstetric	15	0	7	2, or 28.6%	2	0	4	2, or 50%	28	4, or 14.3%		
Gynecologic	40	5, or 12.5%	1	0	1	0	1	1, or 100%	43	6, or 13.9%		
Abdominal operation	26	1, or 3.8%		0				1, or 100%	26	1, or 3.8%		
Irradiation	8	2, or 25%		0		0	0	0	9	3, or 33.3%		
Vaginal operation	3	0		1		1	0	0	5	0		
Irradiation and operation	3	2, or 66.7%		0		0	0	0	3	2, or 66.7%		
Traumatic	1	0		0		0	0	0	1	0		
Neurologic	1	0		0		0	0	0	1	0		
Total	57	5, or 8.8%	8	2, or 25%	3	0	5	3, or 60%	73	10, or 13%		

Failures

Table VII shows the failures in repair.

The following paragraphs summarize these failures.

CASE 1.—The patient, white, aged 18 years, para i-0-0, living in the city, had an operative delivery of a stillborn child. Urethrovaginal fistula occurred in 30 days. She had had no previous operative attempts for closure. Operation was performed at the clinic 5 months after the fistula occurred. Silver wire sutures were used. There was a leak of urine in 11 days. A second attempt by vaginal operation and use of wire sutures also failed. The third attempt, done 3 months after the second failure, was by vaginal operation with use of wire sutures. Leaking occurred 20 days following operation.

CASE 2.—The patient was a Negro, aged 45 years, para i-0-i, living in the city. She was obese and had diabetes. Operative delivery 28 years ago had resulted in a stillborn infant. She had "avulsion" of the urethra and bladder with resultant urethrovaginal fistula. There had been no previous attempts at closure. Operation was done at the clinic 28 years after the fistula appeared. Vaginal operation with use of chromic catgut sutures also failed.

CASE 3.—The patient was white, aged 56 years, para xii-0-vii, rural. She was obese, with hypertensive cardiovascular renal disease, and a large ventral hernia. She gave a history of prolonged labor and operative vaginal delivery of a stillborn child 21 years ago, followed by puerperal infection with abdominal and vaginal operations for drainage of pelvic abscesses. A large vesicocervicovaginal fistula occurred immediately postoperatively. The duration of the fistula was 21 years. One vaginal attempt was made, 4 months after its appearance, to close the fistula. At the clinic, vaginal operation was done with use of chromic catgut. The patient was discharged from the hospital voiding normally. She returned in two months still voiding but with slight leak of urine from the bladder. Refused further treatment.

CASE 4.—Patient was a Negro, aged 33 years, para iii-0-i, rural. She had syphilis which had been inadequately treated. She had had a forceps delivery of a dead child in 1933. Vesicocervicovaginal fistula developed immediately post partum. Operation was done elsewhere 5 months after delivery. It was a failure. Operation was performed here 5 years after the fistula occurred, a vaginal operation with use of chromic catgut sutures. Leaking in 11 days. A second operation was done 4 months later, a vaginal approach with use of wire sutures. Leakage occurred on sixteenth postoperative day. The patient refused a repeat operation.

CASE 5.—The patient was white, aged 54 years, para vi-i-v, lived in the city. She had hypertensive cardiovascular renal disease. The history disclosed an abdominal hysterectomy in 1938 for bleeding. Vesicovaginal fistula appeared 2 weeks after operation. She had 5 attempts at repair elsewhere, and 3 attempts at repair at the clinic. The first attempt was a vaginal operation with use of chromic catgut. Leakage occurred in 16 days. The second was a vaginal attempt with use of silver wire. The fistula repair held for 7 months, then there was recurrence. The third was a vaginal attempt with use of silver wire, with leakage in 14 days. No further attempts were permitted.

CASE 6.—The patient was a Negro, aged 38 years, para i-0-0, rural. She was obese. Previously had received x-ray and radium therapy for squamous-cell carcinoma of the cervix. A vesicovaginal fistula appeared 6 months after irradiation therapy. No attempts at repair were made elsewhere. Duration of the fistula was four years. At the clinic hematometra was evacuated. A renal stone was found. Vaginal operation was performed with the use of chromic catgut. This was a failure. Another operation was refused.

CASE 7.—The patient, a white woman, aged 39 years, para ix-0-vii, rural, was obese and had diabetes. She had a history of intrauterine radium in 1935 for myomas of the

uterus with excessive bleeding. Vesicovaginal fistula developed seven months after radium therapy. Operation was done 16 months after the appearance of fistula, vaginal operation with use of chromic catgut sutures. Leaking occurred on the seventh postoperative day. The patient refused further diabetic regulation and another attempt at repair.

CASE 8.—The patient, a Negro woman, aged 48 years, para i-0-0, was a city dweller. She was obese and had syphilis. She had been treated for squamous-cell carcinoma of the cervical stump with x-ray and radium. A fistula appeared 5 months after termination of irradiation therapy. The duration of the fistula, when she was admitted to the clinic for attempted repair, was six months. This was a vesicocervicovaginal fistula. The operation was vaginal with the use of chromic catgut. This was a failure. She refused repeat operation.

CASE 9.—The patient was an obese white woman, aged 40 years, para i-i-0, who lived in the city. She had diabetes. She was treated elsewhere in 1943 with x-ray and radium for squamous-cell carcinoma of the cervix. In 1949 she had a hysterectomy elsewhere. A vesicovaginal fistula occurred on the eleventh postoperative day. She was seen at the clinic with a fistula of 5 months' duration. Vaginal operation with use of chromic catgut failed with leaking on the eighth postoperative day. The patient refused a second operation.

CASE 10.—The patient was white, aged 73 years, para x-ii-vii, rural. She had an abdominal supravaginal hysterectomy followed by use of cervical radium 14 years before coming to the clinic. Vesicovaginal and rectovaginal fistulas occurred in 6 or 7 months following the procedures. The duration of the fistulas was 14 years. There had been no previous attempts at repair. At the clinic vaginal operation was performed with use of chromic catgut. This was a failure and leakage occurred on the fifteenth postoperative day.

It should be noted that in the 28 obstetric fistulas, which were produced by injury at vaginal delivery, 4 failures occurred; 2 were failures to repair urethrovesicovaginal fistulas and 2 were failures to repair vesicocervicovaginal fistulas. Fifteen vesicovaginal fistulas were repaired without a failure; 7 urethrovesicovaginal fistulas were repaired with 2 failures; 2 urethrovaginal fistulas were repaired with no failure; 4 vesicocervicovaginal fistulas were repaired with 2 failures.

In the 43 gynecologic fistulas, 26 were produced by abdominal operations; 5 were produced by vaginal operations; 8 were produced by irradiation therapy for cancer of the cervix; one was produced in a diabetic patient by irradiation therapy for excessive bleeding from a myomatous uterus; and 3 were produced in patients who had cancer of the cervix treated by irradiation therapy and who then had abdominal operations.

All of the 26 fistulas produced by abdominal operation were vesicovaginal. There was but one failure.

In the 5 fistulas produced by vaginal operations there were 3 vesicovaginal, one urethrovesicovaginal, and one urethrovaginal. All were closed successfully.

In 9 fistulas produced by irradiation therapy, 8 occurred in women with cancer of the cervix. Seven of these 8 were vesicovaginal with one failure, whereas one was a vesicocervicovaginal fistula in which there was operative failure. The other vesicovaginal fistula in this group of nine occurred in a woman with severe diabetes mellitus who developed the fistula seven months after radium therapy for excessive bleeding from a myomatous uterus. The operation was a failure.

In the 3 vesicovaginal fistulas produced in the treatment of cancer of the cervix uteri by irradiation therapy followed by abdominal hysterectomy there were 2 failures. One of these patients had severe diabetes mellitus.

The fistulas were closed successfully in the two patients with vesicovaginal fistulas due to injury other than operative or irradiation trauma.

Thus, in the entire series:

- 57 vesicovaginal fistulas were repaired with failure in five (8.8 per cent)
- 8 urethrovesicovaginal fistulas were repaired with failure in two (25 per cent)
- 3 urethrovaginal fistulas were repaired with no failure
- 5 vesicocervicovaginal fistulas were repaired with failure in three (60 per cent)

In the total series of 73 fistulas there were ten (13.6 per cent) failures.

Postoperative Care

There were no original features of postoperative care. Indwelling catheters were used for periods of time varying from seven to twelve days. Irrigation of the catheters was fairly routine. Attempts were made to keep the urine at a pH of 6.5 or less. The use of chemotherapeutic and antibiotic agents varied with different surgeons.

The patients were allowed to move freely in bed. A few patients were kept lying on their abdomens for varying lengths of time although this practice was not general. It was used more frequently in the patients with fistulas caused by irradiation therapy or by irradiation therapy followed by operation.

Summary

1. A series is reported of 73 consecutive patients with 57 vesicovaginal fistulas, 8 urethrovesicovaginal fistulas, 3 urethrovaginal fistulas, and 5 vesicocervicovaginal fistulas.

2. These patients were admitted in the last 175 months. Operations for repair were done by 5 members of the upper staff and by 18 members of the house staff.

3. There were no deaths in this series. There was no serious postoperative morbidity. There was a failure rate of 13.6 per cent for the entire series of the various types of fistulas.

4. The fistulas are divided into five main groups:

- I. Twenty-eight obstetric fistulas caused by injury at vaginal delivery.
- II. Twenty-six fistulas caused by abdominal operations and 5 fistulas caused by vaginal operations.
- III. Two fistulas caused by trauma which was not of obstetric, gynecologic, or irradiation origin.
- IV. Nine fistulas caused by irradiation therapy in 8 patients with cancer of the cervix and in one diabetic patient with myomas of the uterus and excessive bleeding.
- V. Three fistulas caused by irradiation therapy for cancer of the cervix with the irradiation followed by some type of abdominal hysterectomy.

5. General data for the various groups are presented:

In the series of 73 patients, the oldest was 73 years of age and the youngest was 12 years old.

Durations of the fistulas are given.

In the entire series of 73 patients, 5 (6.8 per cent) had diabetes mellitus.

Three (30 per cent) of the 10 failures in this series of 73 various types of fistulas occurred in obese, diabetic patients. Two (20 per cent) of the 10 failures occurred in patients with syphilis.

Preoperative care and postoperative care are mentioned briefly because we still consider them important.

6. There were 62 unsuccessful operations performed on 31 patients prior to their admission to the clinic; 42 patients had no operations before coming to the clinic. In the clinic 73 patients had 97 operations done for cure in 63 (86.3 per cent) and failure of cure in 10 (13.7 per cent). Ninety-five of these 97 operations were done vaginally and but 2 were done by the suprapubic approach.

7. In the entire series 57 vesicovaginal fistulas were repaired with failure in 5 (8.8 per cent); 8 urethrovesicovaginal fistulas were repaired with failure in 2 (25 per cent); 3 urethrovaginal fistulas were repaired with no failure; 5 vesicocervicovaginal fistulas were repaired with 3 failures (60 per cent). The failure rate for the entire series was 13.6 per cent.

8. In the 9 fistulas which were due to irradiation therapy, and in the 3 due to irradiation therapy followed by some type of abdominal hysterectomy, there were 11 vesicovaginal fistulas with failure in 4 (36.3 per cent), and one vesicocervicovaginal fistula with failure in repair (100 per cent). Therefore, in the 12 fistulas in the irradiation and in the irradiation followed by operation groups, there were 7 successful repairs and 5 (41.6 per cent) failures. Eleven of these 12 patients had cancer of the cervix.

9. In the other group of patients who had not received irradiation therapy, or irradiation therapy followed by some type of abdominal hysterectomy, there were:

- (a) 46 vesicovaginal fistulas with one (2.17 per cent) failure
- (b) 8 urethrovesicovaginal fistulas with 2 (25 per cent) failures
- (c) 3 urethrovaginal fistulas with no failures
- (d) 4 vesicocervicovaginal fistulas with 2 (50 per cent) failures

In short, in 61 fistulas of various types, there were 5 (8.19 per cent) failures.

10. Although the duration of the fistulas and the preoperative and postoperative care may be of great importance in the management of these fistulas, we believe that:

(1) The nature of the injury which caused the fistula, the type of fistula, and its location are the main factors in determining the results of attempted repair.

(2) Fistulas which occur after irradiation therapy and after irradiation therapy followed by some type of abdominal hysterectomy contribute the highest rate of failures.

(3) The ability to mobilize tissues adequately, without destroying blood supply, and to close these tissues carefully and easily in layers are necessary procedures for successful repair.

References

1. Sims, J. M.: *Am. J. M. Sc.* 23: 69, 1852.
2. Emmet, T. A.: *Tr. Am. Gynec. Soc.* 3: 114-134, 1878.
3. Kelly, H. A.: *Bull. Johns Hopkins Hosp.* 7: 29, 1896.
4. Kelly, H. A.: *Bull. Johns Hopkins Hosp.* 10: 115, 1899.
5. Stone, W. S.: *Tr. Am. Gynec. Soc.* 31: 212-219, 1906.
6. Stone, I. S.: *Tr. Am. Gynec. Soc.* 31: 220, 1906.
7. Kelly, H. A.: *Tr. Am. Gynec. Soc.* 31: 225, 1906.
8. Ward, G. G.: *Surg., Gynec. & Obst.* 25: 126, 1917.
9. Judd, E. S.: *Surg., Gynec. & Obst.* 30: 447, 1920.
10. Ward, G. G.: *Surg., Gynec. & Obst.* 37: 678, 1923.
11. Young, H. H.: *Surg., Gynec. & Obst.* 45: 226, 1927.
12. Sears, N.: *AM. J. OBST. & GYNEC.* 18: 267, 1929.
13. Mahfouz Bey, N.: *J. Obst. & Gynaec. Brit. Emp.* 37: 566, 1930.
14. Apajalahti, A.: *Acta obst. et gynec. Scandinav.* 11: 1, 1931.
15. Frank, R. T.: *AM. J. OBST. & GYNEC.* 24: 411, 1932.
16. Ward, G. G.: *AM. J. OBST. & GYNEC.* 25: 1, 1933.
17. Dean, A. L.: *AM. J. OBST. & GYNEC.* 25: 667, 1933.
18. Ward, G. G.: *Surg., Gynec. & Obst.* 58: 67, 1934.
19. Stephenson, G. W., and Masson, J. C.: *Surg., Gynec. & Obst.* 58: 1036, 1934.
20. Schmitz, E. F.: *J. A. M. A.* 104: 1212, 1935.
21. Miller, N. F.: *AM. J. OBST. & GYNEC.* 30: 675, 1935.
22. Phaneuf, L. E.: *AM. J. OBST. & GYNEC.* 31: 316, 1936.
23. Pemberton, F. A., Smith, G. Van. S., and Graves, S. C.: *New England J. Med.* 215: 1170, 1936.
24. Halban, J.: *AM. J. OBST. & GYNEC.* 33: 1073, 1937.
25. Counseller, V. S.: *Texas State J. Med.* 33: 288, 1937.
26. Douglass, M.: *Surg., Gynec. & Obst.* 65: 534, 1937.
27. Franche, O.: *J. d'Urol.* 45: 205, 1938.
28. Mahfouz, N. P.: *J. Obst. & Gynaec. Brit. Emp.* 45: 405, 1938.
29. Babcock, W. Wayne: *South. Surgeon* 8: 34, 1939.
30. Aldridge, A. H.: *AM. J. OBST. & GYNEC.* 37: 985, 1939.
31. Scott, W. W., and Wilson, K. M.: *Surg., Gynec. & Obst.* 69: 663, 1939.
32. Danforth, W. C.: *AM. J. OBST. & GYNEC.* 39: 690, 1940.
33. O'Connor, V. J.: *Surg., Gynec. & Obst.* 70: 826, 1940.
34. Masson, J. C., and Wilson, R.: *Minnesota Med.* 24: 637, 1941.
35. Counseller, V. S.: *Surg., Gynec. & Obst.* 74: 738, 1942.
36. Holden, F. C.: *AM. J. OBST. & GYNEC.* 44: 880, 1942.
37. Latzko, W.: *Am. J. Surg.* 58: 211, 1942.
38. Miller, N. F.: *AM. J. OBST. & GYNEC.* 44: 873, 1942.
39. Phaneuf, L. E.: *Am. J. Surg.* 58: 157, 1942.
40. Counseller, V. S.: *Surg. Clin. North America* 23: 1190, 1943.
41. Phaneuf, L. E.: *Am. J. Surg.* 64: 1, 1944.
42. Roberts, M.: *J. Obst. & Gynaec. Brit. Emp.* 51: 519, 1944.
43. Counseller, V. S.: *New York State J. Med.* 45: 987, 1945.
44. Thomas, G. B.: *J. Obst. & Gynaec. Brit. Emp.* 52: 262, 1945.
45. Thompson, D. J.: *J. Obst. & Gynaec. Brit. Emp.* 52: 271, 1945.
46. Douglas, D. M.: *Brit. M. J.* 2: 78, 1945.
47. Hayes, S. N.: *Surg., Gynec. & Obst.* 81: 346, 1945.
48. Douglass, M.: *Surg., Gynec. & Obst.* 81: 667, 1945.
49. Aldridge, A. H.: *AM. J. OBST. & GYNEC.* 51: 299, 1946.
50. Twombly, G. H., and Marshall, V. F.: *Surg., Gynec. & Obst.* 83: 348, 1946.
51. Scrivner, W. C.: *AM. J. OBST. & GYNEC.* 53: 694, 1947.
52. Ingleman-Sundberg, A.: *Gynaecologica* 123: 380, 1947.
53. Te Linde, R. W.: *Ann. Surg.* 126: 64, 1947.
54. Counseller, V. S.: *South. Surgeon* 13: 752, 1947.
55. Reich, W. J., Wilkery, J. L., and Nechtow, M.: *Urol. & Cutan. Rev.* 51: 566, 1947.
56. Krishnan, R. G.: *J. Obst. & Gynaec. Brit. Emp.* 56: 22, 1949.
57. Phaneuf, L. E., and Graves, R. C.: *Surg., Gynec. & Obst.* 88: 155, 1949.
58. Kantor, H. I., Miller, J. E., and Dunlap, J. C.: *AM. J. OBST. & GYNEC.* 58: 354, 1949.
59. Everett, H. S., Brack, C. B., and Farber, G. J.: *AM. J. OBST. & GYNEC.* 58: 908, 1949.
60. Tyrone, C.: *South. Surgeon* 15: 809, 1949.
61. Malpas, P., Jeffcoate, T., and Lister, U. M.: *J. Obst. & Gynaec. Brit. Emp.* 56: 949, 1949.
62. Harguindey, J. S., and Amezaga, M. M.: *Casa de la Madre*, No. 2, Madrid, 1949.
63. Holloway, H. J.: *AM. J. OBST. & GYNEC.* 60: 30, 1950.
64. Te Linde, R. W.: *AM. J. OBST. & GYNEC.* 60: 273, 1950.
65. Cohn, S., and Weinberg, A.: *AM. J. OBST. & GYNEC.* 60: 363, 1950.
66. Bramhall, T. C., and Marshall, D. F.: *AM. J. OBST. & GYNEC.* 60: 834, 1950.

Discussion

DR. WM. E. STUDDIFORD, New York, N. Y.—Dr. Carter has just presented a series of cases of varying types of vesicovaginal fistulas which, modestly, he calls small but which actually composes one of the largest groups reported in this country in recent years. The proportion of these cases to the general gynecological admissions on his service has not been mentioned. All of his patients were subjected to surgery. As will be seen, the discussion of this report in the light of our experience at Bellevue Hospital is somewhat difficult. It is hard to compare the material of a municipal hospital serving part of a large city population, to that of an institution serving a small city and drawing from extensive rural areas.

Such lesions as observed at Bellevue over the past 16 years have recently been reviewed by Delaplaine. They could be classified as to location and etiology. Under the latter, they were caused by cancer and its treatment, generally of the cervix; to surgical trauma; to obstetrical trauma; and, finally, to unusual factors. As to location, they were classified as vesical, implying a site well above the bladder neck; lesions related to the bladder neck, involving more or less of the urethra; and, finally, pure urethral defects.

Among over 30,000 admissions during this period, 50 instances of fistula were noted. Thirty-eight of them could be classed as vesicovaginal, 10 involved the bladder neck and more or less of the urethra, while two were present in the urethra alone. We were responsible for a minority of these lesions, most of them having occurred in other institutions and many of them having had attempts at repair. We have encountered no fistula that could be classed as cervicovesicovaginal. Did these tracts lead directly into the cervical canal?

As to causation, 21 were related to carcinoma of the uterus, with or without radiation therapy; 20 of them to carcinoma of the cervix, one occurring in a patient with carcinoma of the corpus subjected to radiation and total hysterectomy. All of them were vesicovaginal in type. Fifteen of the latter group were considered to be in terminal condition, some dying within a week of admission. They were not considered suitable for operation. Three refused operation, while one was an uncontrollable psychotic patient. Only one of the fistulas due to carcinoma of the cervix and radiation was operated upon with partial relief. The fistula related to carcinoma of the corpus was cured surgically but the patient died two years later of recurrent tumor. Thus we can show a 50 per cent cure rate on the basis of two cases, a poor showing compared to the results shown by Dr. Carter. Undoubtedly, some selection must be exercised in admitting this group of patients to the Duke Clinic.

Fourteen of these fistulas were due to injury sustained during obstetrical procedures, generally difficult forceps operations. Nine of them were vesicovaginal; 3 involved the bladder neck with total destruction of the urethra; and 2 involved the urethra alone. Of these patients 10 were cured by operation; one was improved, being continent on sitting and lying down; 2 were failures, while one (urethral) was not subjected to surgery because she was symptomless. The only death in this series occurred in this group. This patient had large fibroids and was subjected to a hysterectomy in the hope that the bladder defect might be exposed during the operation and repaired abdominally. The vesical defect was not identified during the procedure.

Twelve fistulas were due to surgical injury, 6 of them being vesicovaginal, while 6 involved the bladder neck and upper urethra. The antecedent operation was most commonly a vaginal plastic or vaginal hysterectomy closely followed by abdominal total hysterectomy. Eight of these patients were surgically cured. Three refused surgical treatment. The only failure occurred in a patient who received radiation therapy for menorrhagia three weeks postoperatively after an apparently successful result.

The three remaining patients showed an unusual etiological background. In one the urethra and bladder neck had been destroyed by lymphogranuloma venereum. She refused operation. The other two were young nulliparas who had received fever therapy for gonorrheal infection by "hotbox" combined with vaginal diathermy. Both were cured by operation.

Of the 50 cases, only 26 were suitable for, or would permit, surgical treatment. Of the 24 due to surgical or obstetrical trauma, 16 were vesicovaginal fistulas with three failures (18 per cent); 7 were lesions of the bladder neck with 2 failures (28 per cent); the repair of the one urethral fistula was successful. These results were obtained in 26 patients by means of 44 operations, the maximum in one patient being 4, a successful result being eventually attained in the latter case. We feel certain that our results in vesicovaginal fistulas would have been improved if certain patients had returned for further surgery. Nevertheless, these figures serve to emphasize the excellent results attained by Dr. Carter and his group.

Dr. Carter has noted a decrease in the frequency with which vesicovaginal fistula is encountered and laments the loss in material. We have not found this to be true since 19 of our cases have been encountered in the past five years. However, we have noted that fistulas due to obstetrical trauma were less frequent while those due to surgical injury were decidedly more frequent. It is our belief that the former group will almost disappear with the increased safety of cesarean section performed after the onset of labor, and that the latter group should markedly diminish with better surgery. At the present time such hopes cannot be held out for fistulas related to carcinoma and its treatment.

I can add but little to what has been said in regard to the preoperative preparation of these patients. Cystoscopic examination certainly should be carried out in every instance, but it should be noted that this method of examination may fail to locate the tract, particularly if it is small. The leak in any container is most easily discovered from the outside rather than the inside. The instillation of a weak solution of methylene blue into the bladder will locate the defect when cystoscopy fails. Examination of the patient in the knee-chest position with the perineum retracted with a Linns speculum often yields valuable information. Surgical repair should not be undertaken soon after traumatic injury has occurred. This will lead to a much greater incidence of failure. Operation should be postponed for at least three or four months, or until all reaction has subsided and the tissues have returned to normal consistency and mobility.

Little was mentioned in regard to operative procedure except that in all but two cases the approach was vaginal. I must suppose that the speaker desires to bring out such details in his discussion. Among the procedures carried out on the patients at Bellevue were the following: 30 vaginal dissections and closures in layers in five of which suprapubic cystotomies were utilized for drainage of the bladder; vaginal flaps were utilized on three occasions in an attempt to close large defects; partial colpocleisis was utilized four times. Transvesical repair was employed on three occasions in one of which the right ureter was transplanted because of its proximity to the tract. In one patient with a large defect of the bladder neck and urethra, both ureters were transplanted into the large bowel. The latter patient is alive, well, and comfortable sixteen years after her operation, although x-ray studies show bilateral hydroureter and hydronephrosis of moderate degree. We have, therefore, exercised a somewhat wider choice of surgical procedures in attacking this problem. Each of these operations has proved of value in particular situations.

Three fundamental principles must be carried out in order to assure as much as possible the operative cure of vesicovaginal fistula: (1) careful dissection and separation into layers of the tissues adjacent to the tract, and closure, without tension, in layers, inverting the bladder mucosa, by fine interrupted sutures; (2) prevention of infection; and (3) decompression of the bladder by continuous drainage of urine until healing has been attained.

Continuous drainage is secured usually by the use of some form of indwelling catheter. This is quite satisfactory, providing the operative closure lies well above the bladder neck and does not come in contact with the head of the catheter. However, when the closure is at the bladder neck, often involving the upper urethra, the catheter may be harmful, both from mechanical irritation of the sutured wound and because it must produce some increase in tension on the sutures. For these reasons in this type of case we have used drainage by means of a soft rubber sump placed in the bladder by abdominal cystotomy prior to the vaginal repair. We have also found that, with the pa-

tient placed in the Kraske position, the perineum retracted with or without episiotomy, and with a simple catheter in the urethra, much better exposure could be obtained and the lesion could be defined and dissected more easily. Suprapubic drainage was carried out for at least two weeks, using the electric pump designed for the Wangenstein apparatus attached to a simple catheter placed within the sump. Thus the area of repair was put at complete rest. Five consecutive cases of bladder neck fistula have been treated successfully by this method, four of them on the Bellevue service. I would like to ask Dr. Carter if this type of drainage has been used on any of the cases in his report.

DR. VIRGIL S. COUNSELLER, Rochester, Minn.—There are so many interesting phases for discussion about the causes of fistulas and the treatment of different types of vesical fistulas that one hardly knows which ones to stress the most. Although this series reported by the authors is not a large one, it does certainly give an excellent review of the procedures as conducted in their clinic. The results coincide with those reported throughout the country in general. The small number of urinary fistulas encountered following difficult obstetric deliveries is observed in most clinics throughout the country and certainly speaks well for the improved management in difficult obstetric problems compared to a few years ago. On the other hand, the gradual increase of the urinary fistulas due to gynecologic operative trauma and those from radiation therapy for carcinoma of the cervix and from radical operations for carcinoma of the cervix should be of considerable concern. Those fistulas following operations for benign lesions of the pelvic organs can mean only one thing, and that is that greater care must be utilized in doing difficult pelvic operations, particularly in benign lesions.

It is of interest that during the past five years, not one of the 28 patients here reported had a ureterovaginal fistula. It seems to me that we are seeing an increasing number of ureterovaginal fistulas following total abdominal hysterectomy for benign lesions. This becomes a very complicated problem but one about which I think some very definite facts can be stated. The fistula is usually low down near the ureterovesical juncture. If the ureter has had adequate drainage, there will probably be no disturbance in the upper part of the urinary tract. The treatment in this instance would be reimplantation of the ureter into the bladder just above the ureterovesical orifice, and the simpler the technique of anastomosis the better will be the result. I would suggest that a urethral catheter, about a No. 12 or No. 14, be placed in the bladder and that, when the ureter is cut off and the bladder is opened, this catheter be threaded up the ureter for a distance of 4 or 5 inches. The ureter is then threaded into the bladder and sutured in position with four or five stitches just catching the adventitia of the ureter and bladder wall. The catheter then must be sutured to the labia so as to hold it in place for at least ten to fourteen days. Most ureters transplanted in this fashion will heal and function satisfactorily. If there has been evidence of infection of the upper part of the urinary tract with resulting ureterectasis, pyelectasis, hydronephrosis, cortical abscesses, chills and fever, it is infinitely safer to perform nephrectomy than it is to reimplant the ureter into the bladder. This decision is justified if a sound kidney exists on the opposite side.

The time interval between the original accident and the first attempt at repair is very important. A minimum of four months should elapse before attempted repair should be made. I have arbitrarily set this period of time because it seems to me that this amount of time is required for all inflammation and infection to subside. Also, it is important for the blood supply to have adequate opportunity to regenerate. I am sure that it is a mistake, when urinary fistula is discovered during the postoperative convalescence following either an abdominal or a vaginal operation, for the patient to be returned to the operating room for investigation of the leakage. There is nothing that one can do about it which would be of value except to satisfy one's curiosity that a fistula does exist and perhaps its location might be observed. Certainly, suturing it at this stage would result in a high incidence of recurrences. Furthermore, when a recurrence develops following a primary repair, then at least four months more should elapse before the second attempt is made to close the fistula. I feel quite sure from my experience, at least, that if these rules are observed a higher incidence of cure will be obtained when subsequent repairs become necessary.

The location of vesicovaginal fistulas always interests me and I have wondered why the fistula should be located so frequently in the midline behind the trigone. I have come to the opinion that it is due to the effort of the surgeon to place clamps on the vagina during a total hysterectomy. It is so easy to injure the bladder in the midline in this fashion, or to place a suture through the bladder when one is closing the vaginal vault. It is for this reason that I teach my students who are assigned to my surgical service that a clamp should never be placed on the vagina in performing a total hysterectomy. The vagina is to be opened posteriorly and then the cervix can be cut around, leaving the vagina open. The bladder is carefully observed as the vaginal vault is closed. The question of pelvic infection from an open vagina is not the problem that it was previously thought to be, particularly if there has been adequate preparation. A fistula which is located near the ureterovesical orifice is nearly always due to a suture and not to a direct cut of the bladder. This comes about by faulty mobilization of the ureterovesical orifice because this is the most fixed point in the entire urinary tract.

Recurrences or failures are usually in direct proportion to the number of repairs, and I note that the authors had their worst troubles with those fistulas produced by radiation therapy for carcinoma of the cervix. Our experience at the Mayo Clinic is the same. In these situations I think that even more time should elapse between the occurrence of the fistula and the first attempted repair. We should not attempt repair until we are reasonably sure that there will be no recurrence of the cancer and this is a minimum of three years. If the base of the bladder, trigone, and urethra have been destroyed, the ureters may be transplanted at an earlier date, or perhaps bilateral ureterostomies or nephrostomies could be done for the patient's comfort.

I have always believed that the method of approach should be the vaginal route. Nearly all of these fistulas can be mobilized through the vagina. There are some exceptions, however. Fistulas which have been repeatedly repaired may result in so much scarring that the vaginal vault becomes fixed and immobile. This situation is very likely to exist when both vesicovaginal and rectovaginal fistulas are present. There has occurred more inflammatory reaction in these instances than in vesicovaginal fistula alone.

The authors have stressed the importance of preoperative study, especially of the bladder and the upper part of the urinary tract. The study of the bladder should include a search for multiple fistulous openings, because a hidden fistula may be the source of continued vaginal leakage. Multiple fistulas are not uncommon.

Acidification of the urine is most important, and the judicious use of antibiotics is very helpful. I prefer to maintain the hydrogen-ion concentration at 5.5 or less. If the urine becomes only slightly alkaline, mucus will collect in the bladder and the catheter frequently will become occluded. This I consider a danger signal. If mucus or sediment appears in the catheter, the catheter should be changed immediately. The frequency with which this is required will depend on the acidity or alkalinity of the urine.

I doubt whether it is wise to ambulate these patients as early as other surgical patients. More time is required for most of these fistulas to heal. Then, too, we must remember that we are closing a hole in a viscus that contains water all the time, and if there is any way to keep urine away from the suture line for ten to fourteen days by any position or method it should be done.

DR. FRANK R. SMITH, New York, N. Y.—Any of us who do radical surgery in carcinoma are bound to have urinary accidents. Formerly, I felt as Dr. Counseller does, that probably the best plan is to take the kidney out. I have come to feel that we can save a great many of these kidneys. We have had some patients who have had ureteral damage and we have had to sacrifice the lower part of her ureter. Several have been treated with the procedure in which a bladder flap is turned down in the same manner as a Janeway gastrostomy and the ureter implanted into this flap. I believe we do not use often enough suprapubic vesicle drainage when we do ureteral implantations. It is the biggest safety factor when we do repairs of bladder fistulas. Too many times we try to get away with not doing a suprapubic drainage, which the urologists have known for a good many years is a safety procedure but we have been very hesitant in adopting it.

DR. HOUSTON S. EVERETT, Baltimore, Md.—I have been much interested in this subject of vesicovaginal fistulas for a long time. There is one group that Dr. Carter did not include in placing the blame for these fistulas, and that group is the urologists. Fistulas of the vesicourethrovaginal type not infrequently result from the injudicious use of the resectoscope upon the female vesical neck. I have seen several patients with fistulas of this type and they are extremely difficult to manage. The fistula can usually be closed easily, but total incontinence persists because the sphincter has been destroyed. We then have to resort to some such procedure as the strap operation described by Aldridge and Studdiford. Such procedures are technically difficult in these cases because of the thinness of the tissue underneath the urethra. I have wondered if Dr. Marchetti's procedure would be of benefit in curing the incontinence in such patients. I have not yet had an opportunity to try it in this type of case.

As has been emphasized, the fistulas resulting from irradiation are often the most difficult to close because of the scarring and poor blood supply of the surrounding tissues, but sometimes the patient can be relieved of her distressing condition without actually closing the fistula. We encountered one patient who, twelve years after successful treatment of carcinoma of the cervix by irradiation, developed both vesicovaginal and rectovaginal fistulas. Both were quite large and the tissues were in no condition to permit repair. A colostomy was done first, and later the vulva was completely closed even occluding the urethra, so that subsequently feces were passed through the colostomy and urine through the anus.

In another patient with a very large defect in the upper vesicovaginal septum resulting from irradiation, a ring of mucosa completely around the vagina below the level of the fistula was denuded and sutured in three layers, thus converting the upper vagina into a part of the bladder. After this the patient was completely continent.

DR. LOUIS E. PHANEUF, Boston, Mass.—Being interested in the subject of vesicovaginal fistula, so well presented by Dr. Carter, I have looked up my personal series of cases which in number is 43. The methods employed in closing these fistulas were the following: Sims' classical operation, 5 cases; suprapubic extraperitoneal closure and later vesical implantation of right ureter, one case; vaginal flap method, 22 cases; colpocleisis, one case; colpocleisis and later opening of vagina and transplantation of ureters in the sigmoid, one case; implantation of right ureter in the bladder and intravesical closure of vesicovaginal fistula, one case; intravesical closure, 4 cases; vaginal flap method and reconstruction of the urethra, 2 cases; transplantation of ureters in the sigmoid, 6 cases.

In the 43 cases of vesicovaginal fistulas, 16 patients had suprapubic drainage, 5 patients after the intravesical operation and 11 patients after the vaginal procedure. All fistulas were closed, one by another surgeon, after I had failed twice. One patient had multiple fibromyomas and a vesicovaginal fistula the size of a silver half-dollar following a high forceps delivery. A panhysterectomy and bilateral salpingo-oophorectomy were performed at the Carney Hospital on June 18, 1946. On Oct. 18, 1946, she had an intravesical closure of the fistula. On Jan. 2, 1947, examination revealed slight intermittent leakage of urine from the right of the scar which was hidden behind the symphysis pubis. She returned to California and was referred to Dr. Frank Hinman of San Francisco, who stated that in June, 1947, cystoscopy revealed a small fistulous opening in the bladder, about 4 mm. in diameter, in the superior portion of the scar on the right side. A functioning right ureter was not found. He felt hopeful that this remaining fistula could be closed successfully.

DR. CARTER (Closing).—As I stated, this paper was in no way concerned with ureterovaginal fistulas caused by operation. We expect to report the ureterovaginal fistulas later.

Perhaps in our fistulas following irradiation therapy we will have to modify our operative technique and perhaps we should use suprapubic drainage more frequently.

RESULTS OF THE TREATMENT OF OVARIAN MALIGNANCIES*

CLYDE L. RANDALL, M.D., AND DONALD W. HALL, M.D., BUFFALO, N. Y.

(From the University of Buffalo and the Buffalo General Hospital)

REPORTED results of treatment add confusion to the usually depressing picture of ovarian malignancy. The literature was ably reviewed by Munnell and Taylor¹ in 1949. They emphasized variations as noticeable as the 65.4 per cent five-year survivals among 143 patients reported by Counseller² in 1940; and a five-year survival rate of 15.5 per cent among 154 cases reported by Meigs³ in 1940; or Taylor and Greeley's⁴ 15.2 per cent five-year survivals among 138 cases reviewed in 1942.

The literature also records adequate discussion of the factors that probably account for such variations in survival rates. To classify all papillary cystomas, particularly those considered "borderline" in some groupings, as malignant tumors of the ovary, greatly increases the incidence of long-time survivals. When reporting a five-year survival rate, reviewers may include such entities as granulosa-cell tumors, dysgerminomas, and teratomas as well as metastatic or secondary malignancies. However, when such rarer tumors are excluded from the calculation, the reported incidence of five-year survivals among primary "carcinomas of the ovary" shows a consistency not evident at first glance.

A recent review indicates that in 16.2 per cent of the women operated upon for ovarian tumors in the Buffalo General Hospital since 1936, the neoplasm proved to be malignant. Among 218 tumors first recognized in women over 50 years of age, 131, or 60 per cent, were malignant neoplasms.

Material

During the 15 years, 1936 to 1950 inclusive, at the Buffalo General Hospital, a total of 237 ovarian malignancies included 228 carcinomas, four sarcomas, three fibroblastomas, and one mesonephroma. During the same period, there were, in addition, 16 granulosa-cell tumors, 6 dysgerminomas, and 28 teratomas. Only two of the teratomas were histologically and clinically malignant. Eight struma ovarii, 6 Brenner tumors, one thecoma, and one interstiteoma were considered benign.

Follow-up studies indicate that an over-all cure rate would be of no prognostic value as far as any individual type of ovarian malignancy is concerned. Five-year survival rates are, therefore, reported only in terms of the entities generally recognized among such a variety of neoplasms.

Primary Carcinomas of the Ovary

Unfortunately, primary carcinomas of the ovary comprise the largest group of ovarian malignancies and are highly malignant. Correspondence

*Presented at the Sixty-second Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 8, 1951.

with referring doctors and relatives and the help of a number of the Staff has enabled us to follow 95 per cent of the patients with ovarian malignancies operated upon in this Hospital since 1940. Among 111 cases of primary carcinoma of the ovary treated during 1936 to 1942, inclusive, 16 women, or 14.4 per cent, survived more than 5 years. However, among 89 primary carcinomas of the ovary operated upon during the years 1941 to 1946, inclusive, only 6 women, or 6.7 per cent, lived more than 5 years.

In addition to this low rate of five-year survivals, two other observations emphasize the ineffectiveness of the treatment given. Among the patients known to be dead, 69 per cent died within less than a year from the date the diagnosis was first established. Moreover, among the few known to have survived more than five years, 70 per cent are already known to have succumbed to carcinomatosis—regarded as a recurrence of their ovarian malignancy.

Secondary or Metastatic Ovarian Tumors

It has been frequently noted that the ovary is peculiarly susceptible to metastatic involvement. While extension from the uterus is not surprising, metastatic involvement from the breast or stomach is found not infrequently in what, at first glance, suggests a primary neoplasm of the ovary. We have noted no explanation of the fact that while primary ovarian malignancies readily and early shed implanting cells from their surfaces onto adjacent peritoneum—with resulting adhesions and early involvement of the omentum—secondary carcinomas of the ovary do not display the same tendency.

Bose⁵ has called attention to data indicating that secondary or metastatic tumors of the ovary are not slow growing as originally implied by Krukenberg, and states that he could find no published case in which the patient had recovered. However, Daley⁶ has recently reported one case of histologically typical Krukenberg tumor removed from the pelvis of a patient who has remained well for a considerable period of time, with no demonstrable evidence of a primary growth.

TABLE I. METASTATIC CARCINOMA IN OVARY—10 CASES

A.			
AGE OF PATIENT	PRIMARY TUMOR	REMOVAL OF PRIMARY TUMOR TO REMOVAL OF SECONDARY GROWTH IN OVARY	SURVIVAL AFTER REMOVAL OF METASTATIC TUMOR IN OVARY
61 years	Cervix, adenocarcinoma	10 months	2 months
40 years	Cervix, squamous-cell carcinoma	4 years	1 week
70 years	Cervix, squamous-cell carcinoma	9 years	1 month
51 years	Breast	3 years	10 months
54 years	Breast	11 years	7 months
B.			
AGE OF PATIENT		PERIOD OF OBSERVATION	STATUS
16 years	Krukenberg	3 months	Deceased
37 years	Krukenberg	14 months	Deceased
38 years	Krukenberg	3 months	Deceased
39 years	Krukenberg	3 months	Deceased
37 years	Krukenberg	At autopsy	Deceased

Table I illustrates sources of metastatic tumor which we have noted in the ovary. One was secondary to adenocarcinoma of the cervix, two were metastatic 4 and 9 years after treatment of squamous-cell carcinomas of the cervix, and two were secondary to carcinoma of the breast.

It is evident that, in our experience, Krukenberg tumors are usually found in patients dying of gastric cancer. In all ten cases of secondary ovarian

malignancy observed, the patients died within a few months after the ovarian growth was removed.

Karsh⁷ has recently reported 72 cases of metastatic malignancy of the ovary discovered at autopsy during a period when 10,000 postmortems were performed. He emphasized that in half the cases the ovaries did not appear grossly enlarged, and that metastatic involvement was bilateral in two-thirds of the patients. The primary tumor most frequently noted by Karsh was carcinoma of the breast; gastric carcinoma was second. Carcinoma of the cervix was a frequent source by direct extension, but the ovaries were rarely involved by the purely metastatic spread of endometrial or cervical malignancy. Karsh was also impressed by the fact that breast carcinoma metastasizes to the ovary more often before the menopause, although the ovaries of younger, premenopausal women were rarely involved by the metastasis of a uterine or cervical malignancy.

Miscellaneous Rarer Types

Certain rarer malignant tumors are occasionally found in the ovary and, of these, sarcomas are the most frequent. At the Buffalo General Hospital, we found that during the fifteen-year period surveyed, 4 tumors of the ovary were classified as sarcomas. All occurred in girls 20 years of age or younger, and all proved rapidly malignant. One tumor, classified as a mesonephroma, was likewise malignant.

Teratomas

Only one of 170 dermoids removed during the years 1936 to 1950 was found to harbor a squamous-cell carcinoma. The patient has remained well and free of appreciable recurrence for six years after removal of the growth.

No example of carcinoid has been noted in the tumors classified as dermoids or teratomas. While adult teratomas might be grouped with the tumors whose malignant potentialities are unpredictable, this is certainly not the case with the so-called embryonic teratomas, whose malignant character is usually unquestioned. Only two women in this series, aged 61 and 68 years, had the embryonic type of teratoma, and both tumors exhibited a rapidly fatal course. None of the adult type followed have exhibited evidence of recurrent tumor or of metastatic malignancy. However, Smeltzer⁸ has advised treating solid teratoma of the ovary, when it occurs in a prepuberty or adolescent girl, as a highly malignant tumor. Reviewing 32 published cases, he reports that 65 per cent exhibited an early recurrence at the site where an apparently well-encapsulated and pedunculated tumor had been removed. Smeltzer urges, therefore, that solid teratomas in such young individuals should be excised as radically and widely as an adenocarcinoma in the pelvis of an older woman. In estimating the prognosis when teratomas appear malignant, several reports have emphasized that a relative preponderance of neurogenic elements foretells a particularly malignant course, whether that preponderance is exhibited in the primary tumor or in a recurrent or metastatic growth.

Granulosa-Cell Tumors

The reported incidence of granulosa- and theca-cell tumors varies. Spencer and Zeph⁹ have reported that 2.4 per cent of ovarian tumors studied at the University of California Hospitals were classified as granulosa cell, while Hodgson¹⁰ found 62 among 3,800 ovarian tumors removed at the Mayo Clinic an incidence of 1.63 per cent.

We have observed 14 granulosa-cell tumors among 1,112 ovarian neoplasms removed, an incidence just below 1.2 per cent. Ten of these patients have been followed for more than five years, but Table II indicates the neces-

sity for a long-time follow-up before the malignant potentiality of granulosa-cell tumors can be evaluated. Two patients with grossly encapsulated but histologically malignant granulosa-cell tumors received postoperative x-ray therapy and were surviving without appreciable recurrence when their deaths occurred from causes unrelated to the tumor (Table II). Two women died 14 and 19 months after "carcinomatosis" of the abdomen was found to show the histologic picture of granulosa-cell carcinoma. Both of these patients received x-ray therapy with little appreciable benefit, unless a one and one-half year survival with abdominal carcinomatosis should be credited to irradiation. Hodgson,¹⁰ after a study of 62 granulosa-cell tumors removed at the Mayo Clinic, states that they were unable to evaluate postoperative irradiation in that series.

TABLE II. GRANULOSA-CELL TUMORS (10 FOLLOWED MORE THAN 5 YEARS)

AGE OF PATIENT	DEATH DUE TO OTHER CAUSES	DEATH DUE TO TUMOR	PERIOD WITHOUT EVIDENT RECURRENCE
42 years	Cardiac after 7½ years		
76 years	Carcinoma of antrum after 5½ years		
72 years		at 14 months	
47 years		at 19 months	
58 years		at 5½ years	
45 years		at 7½ years	
48 years			5½ years
66 years			7½ years
41 years			8 years
40 years			10¼ years

Jones and Te Linde¹¹ found recurrence of supposedly benign granulosa-cell tumors 15, 16, and 19 years after oophorectomy—an observation that would seem to pass on to the next generation a decision regarding the malignancy of these tumors. Moreover, it should not be forgotten that even if the primary granulosa-cell tumor does not become malignant, there is considerable evidence that adenocarcinoma may develop in the uterus—if the estrogen level maintains a proliferating endometrium over a long period of time.

Brenner Tumors

I have been under the impression that Brenner tumors are benign, but J. Montgomery¹² included this tumor in a review of 107 "malignant tumors" of the ovary and Sirtori and Bussolati¹³ recently suggested that a Brenner tumor should be regarded as an epithelioma, for it may present "cancerous characteristics." However, in 1939, Smith and Pettit¹⁴ stated that no tumor considered a Brenner type had been recorded in the literature to exhibit a clinically malignant course. Likewise, Dockerty and McCarthy¹⁵ found no evidence of malignancy among 10 Brenner tumors observed at the Mayo Clinic.

TABLE III. BRENNER TUMORS—6 CASES

AGE OF PATIENT	PERIOD OF OBSERVATION	ADDITIONAL PELVIC SURGERY	RADIATION	STATUS
36 years	8 yr. 1 mo.	0	0	Alive and well
58 years	8 yr.	0	x-ray	Alive and well
42 years	6 yr. 11 mo.	0	0	Alive and well
28 years	6 yr. 7 mo.	0	0	Alive and well
43 years	6 yr. 4 mo.	0	0	Alive and well
57 years	Lost	—	—	?

Certainly, Table III, reviewing 5 cases followed more than 5 years, would seem to indicate a benign course.

Dysgerminomas

No optimism is justified regarding the prognosis when dysgerminomas are discovered. Mazel¹⁶ recently stated that 250 cases have been reported in the literature. Novak and Gray¹⁷ at one time advised that all cases be considered as highly malignant as ovarian cancer—that wide excision was indicated with no consideration for the possibility of future childbearing. Since many of these cases occur in girls and young women, this latter point is quite important. Seegar¹⁸ reviewed 79 cases of dysgerminoma in which the five-year survival rate approximated 60 per cent, but Pedowitz and Grayzel¹⁹ recently reported 17 cases with a five-year survival rate of only 12.5 per cent.

TABLE IV. DYSGERMINOMAS—6 CASES

AGE OF PATIENT (YEARS)	PERIOD OF OBSERVATION	RADIATION	STATUS
70	10 months	X-ray	Deceased
48	9 months	X-ray	Deceased
26	8 years	X-ray	Alive and well
20	2 months	0	Deceased
20	5 years	0	Alive and well
18	4½ years	X-ray	Deceased

Our own experience with this neoplasm is summarized in Table IV. The case of an 18-year-old girl is of particular interest. After the abdomen was first opened she was given intensive roentgen therapy when biopsy of a football-sized tumor of the ovary was reported to show typical dysgerminoma. Several months later, the tumor had become much smaller, the pelvis seemed movable, and a panhysterectomy was performed. For 4½ years periodic follow-up examinations did not reveal appreciable recurrence until x-ray films at the time of a fracture indicated widespread metastasis. At autopsy the tumor, metastatic in bone, resembled the primary dysgerminoma removed nearly five years before. Two other patients, operated upon since that time, have married since their tumors were removed, and one not irradiated has delivered at term. In each of the latter instances, the pelvis seemed free of neoplasm except for the involved ovary and only the one ovary was removed. At least in such limited experience, there seems little evidence that a more radical treatment would be worth while. Perhaps normal life may as well continue for these girls for as long a time as the neoplasm will permit, without making their remaining years miserable by extensive surgery and irradiation which may still miss unappreciable foci of tumor.

Comment

Statistics²⁰ from the Division of Cancer Control, Department of Health of the State of New York, enable us to visualize the relative malignancy of lesions arising in the cervix, fundus, and ovary. During the years 1945, 1946, and 1947, physicians in the State reported to the Division 26.7 new cases of carcinoma of the cervix, 14.6 cases of fundal cancer, and 11.28 malignancies of the ovary per 100,000 women in the population. However, this ratio is not duplicated when we review the causes of death as recorded in the Office of Vital Statistics for the years 1948 and 1949. Here we see carcinoma of the cervix, the recorded cause of death for 14.3 women per 100,000, as compared to 7.4 deaths due to fundal cancer, and 10.4 deaths due to malignancies of the ovary.

No statements regarding the ineffectiveness of our present-day treatment of ovarian malignancy could be more impressive than the statistics from Albany. It is evident that among each 100,000 women in upstate New York,

11.3 cases of ovarian cancer are discovered each year, and that during each year 10.4 deaths per 100,000 are due to malignancies of the ovary.

The relative malignancy of ovarian neoplasms is clearly indicated in Table V. The average number of deaths occurring each year compared with the average number of new cases reported per year suggests an appreciable incidence of "cures" among women treated for cervical or endometrial cancer. On the other hand, actual figures indicate that each year, in upstate New York, 88.4 women die of ovarian cancer per each 100 new cases reported.

The obvious approaches to the problems of ovarian malignancy have been thoroughly explored. Earlier diagnosis seems the only solution, yet every review emphasizes the relatively short period of symptoms prior to recognition of the tumor and it appears evident that real improvement can be expected only when ovarian neoplasms are discovered in an asymptomatic stage.

TABLE V. NEW YORK STATE (EXCLUSIVE OF NEW YORK CITY)
1948-1950 INCLUSIVE

SITE	AVERAGE NUMBER NEW CASES PER YEAR	AVERAGE NUMBER DEATHS PER YEAR	RATIO: DEATHS PER 100 NEW CASES OF CANCER
Cervix uteri	961	485.5	50.5
Fundus uteri	559	251.5	45
Ovary	400	353.5	88.4

Ten years ago, H. S. Crossen²¹ emphasized the desirability of recognizing ovarian neoplasms in an early phase of development. He urged careful palpation of the ovaries every time the pelvis could be examined, and advised the prophylactic removal of ovaries whenever the abdomen was opened and the patient "past 43" years of age. In this connection, it is well to recall that Statistics²⁰ from the Division of Cancer Control at Albany indicate that 30.4 females among each 100,000 are developing ovarian malignancies under 45 years of age, whereas, 281.9 cases can be expected to develop among 100,000 women between their forty-fifth and eighty-fifth years.

These data seem to suggest that when prophylactic removal of ovaries is to be considered at age 45 years, we should take into consideration the fact that no more than three women per 1,000 will develop ovarian malignancy—even if they live another forty years. Because of this low incidence, many continue to question the advisability of removing normal ovaries as a cancer-preventing measure.

Analyzing the factors that seem to account for improved results, Taylor,²³ Helsel,²⁴ Bonini,²⁵ and Montgomery,¹² have particularly emphasized the prognostic significance of clinical grouping and operability. To date, no endocrinologic or chemotherapeutic measures have proved effective in the treatment of these neoplasms.

Irradiation seems to have been given an adequate trial, but the majority of reports emphasize the apparent effectiveness of postoperative irradiation in an occasional and otherwise unexplained long-time survival. The effectiveness of roentgen therapy is not very impressive when an appreciable series of irradiated cases is compared with an equal number in which roentgen therapy was not used. However, we believe that the effect of irradiation is unpredictable and that a therapeutic trial is always indicated. Meigs³ and others have pointed out the greater effectiveness of irradiation if the carcinoma is of the cystic variety. It is also generally agreed that radiation *may* literally melt the bulk of an apparently inoperable tumor to a degree making operative removal possible and more effective. On the other hand, in many instances of

ovarian carcinoma, the bulk of the tumor seems but little affected by intensive irradiation. Many share Pemberton's²⁶ view that roentgen therapy slows the reformation of ascitic fluid. However, it should also be remembered that surgical removal of the omentum often accomplishes more than postoperative radiation to reduce the bulk of the abdominal mass.

Preoperative irradiation has been repeatedly recommended, but this diagnosis is difficult to establish without a laparotomy. Moreover, 40 per cent of the ovarian tumors we discover at operation in women past 50 years of age prove to be benign. The possibility of establishing a definite diagnosis by paracentesis is attractive, but laparotomy is usually necessary to identify the source of the "carcinomatous," "anaplastic," or "blastomatous" cells described in the fluid withdrawn. There is, therefore, reason to use preoperative irradiation in the manner recommended by Parks,²⁷ who employed an initial laparotomy to establish the diagnosis, followed by a full course of intensive irradiation before any attempt was made to remove the tumor. Parks' observations suggest that operability might often be improved by such roentgen therapy. Since the prognosis is better when the primary tumor is "operable," if preoperative irradiation can reduce an advanced Clinical Group 2 or 3 lesion until it fulfills the criteria of the clinically favorable Group 1 tumors, noticeably improved results should be realized. Certainly, such "planned therapy" should be given a more extensive trial. Irradiation might not affect all patients as dramatically as described by Parks in the three cases reported—but this suggested plan of treatment seems to offer more possibilities than any other regimen recently proposed.

Schumann²⁸ and Meigs³ have advised more radical operative procedures in an attempt to remove malignancies of the ovary. The possibility that wider excision and radical surgery might offer a means of improving our results has always seemed unlikely, since nearly 50 per cent of reported cases are so advanced when the abdomen is first opened as to warrant a diagnosis of carcinomatosis. In series after series reported, in 40, 50, and 60 per cent of cases, when the abdomen was first opened, only a biopsy seemed justified. Nevertheless, for several years we have attempted to improve our own results by more extensive dissections of pelvic viscera, with extirpation of sigmoid and the entire pelvic peritoneum in some cases. In all instances the tumor appeared inoperable and the only benefit anticipated was that of greater palliation—but this proves a most difficult basis upon which to evaluate treatment.

That such wider primary excision would accomplish little more than palliation is evident if we consider the manner in which most malignancies of the ovary prove fatal. Reviewing the causes of deaths among 61 women dying of ovarian malignancy in the Buffalo General Hospital, we found little to suggest any methods by which death could have been postponed or longer palliation achieved. Thirty-seven, or 60 per cent, of the 61 women died of generalized carcinomatosis or of intestinal obstruction. In the first group, malignancy was too far advanced at the time of a first laparotomy for a pelvic extirpation to affect the rapidly fatal course. In the second group, obstruction usually occurred as a result of a matting together of tumor-thickened loops of small bowel above the segments that would have been excised along with the primary mass in the pelvis. Twenty per cent of the deaths are associated with risks that could scarcely be expected to decrease if more prolonged and radical dissections are to be attempted. With better preparation of patients and optimal utilization of the supportive measures now available, the possible complications of prolonged surgery must still be weighed against the greater degree of palliation that might be realized by a wider excision of involved viscera.

Conclusions

Prompt and adequate investigation of preclimacteric and postmenopausal bleeding has provided an effective means of assuring early diagnosis when carcinoma develops in the endometrium. Periodic examinations and routine employment of the cytologic method assure detection of cervical malignancy in an early "curable" stage. It is evident that, to date, there has been proposed no method of detecting ovarian malignancy in a similarly favorable stage.

Malignant tumors of the ovary are a threat greater than is suggested by the attention given them in gynecologic literature. Relative incidence alone warrants the attention given carcinomas arising in the cervix and endometrium, but a review of the tumors responsible for deaths due to pelvic cancer reveals ovarian malignancies as a major and wholly unsolved problem.

In cases of ovarian malignancy, it would be unfortunate if operators should view the opened abdomen only in terms of the resectability and curability of the lesion. While palliation is not the goal of the surgeon, we should not be satisfied with less.

Exploratory laparotomy to establish the diagnosis, followed by intensive irradiation, may improve the operability in many cases. Wider resection to remove sources of impending obstruction and debilitating pain should at least accomplish a degree of palliation not realized in the past.

Statistics reporting the relative annual incidence of new cases and of deaths due to malignancy of the cervix, fundus, and ovary were provided by Dr. Paul R. Gerhardt, Director, and Irving D. Goldberg, Biostatistician, of the Bureau of Cancer Control, Albany, N. Y.

References

1. Munnell, E. W., and Taylor, H. C., Jr.: *AM. J. OBST. & GYNEC.* 58: 943, 1949.
2. Counseller, V. S.: *AM. J. Surg.* 49: 284, 1940.
3. Meigs, J. V.: *Surg., Gynec. & Obst.* 71: 44, 1940.
4. Taylor, H. C., Jr., and Greeley, A. V.: *Surg., Gynec., & Obst.* 74: 928, 1942.
5. Bose, Sudhir: *Indian M. Gaz.* 80: 255, 1945; *Quart. Review (abst.)* 3: 566, 1946.
6. Daley, Doreen: *Proc. Rural Soc. Med.* 34: 769, 1946; *Quart. Rev. (abst.)* 5: 491, 1947.
7. Karsh, Jamil: *AM. J. OBST. & GYNEC.* 61: 154, 1951.
8. Smeltzer, Merrill: *AM. J. OBST. & GYNEC.* 41: 616, 1941.
9. Spencer, J. A., and Zeph, J. R.: *AM. J. OBST. & GYNEC.* 54: 281, 1947.
10. Hodgson, J. E., Dockerty, M. B., and Mussey, R. D.: *Surg., Gynec. & Obst.* 81: 631, 1945.
11. Jones, G. E. S., and Te Linde, R. W.: *AM. J. OBST. & GYNEC.* 50: 691, 1945.
12. Montgomery, J.: *AM. J. OBST. & GYNEC.* 55: 201, 1948.
13. Sirtori, C., and Bussolati, C.: *Tumori, Milano* 27: 508, 1941; *Internat. Abstr. Surg.* 84: 343, 1947.
14. Smith, G. Van S., and Pettit, R. D.: *AM. J. OBST. & GYNEC.* 38: 156, 1939.
15. Dockerty, M. B., and McCarthy, W. C.: *AM. J. OBST. & GYNEC.* 37: 703, 1939.
16. Mazel, M. S.: *AM. J. OBST. & GYNEC.* 53: 1036, 1947.
17. Novak, E., and Gray, L.: *AM. J. OBST. & GYNEC.* 35: 925, 1938.
18. Seegar, G. Emory: *Arch. Surg.* 37: 697, 1938.
19. Pedowitz, P., and Grayzel, D. M.: *AM. J. OBST. & GYNEC.* 61: 1243, 1951.
20. Division of Cancer Control, Dept. of Health, State of New York: *Personal Communication.*
21. Crossen, H. S.: *J. A. M. A.* 119: 1485, 1942.
22. Taylor, H. C., Jr.: In Meigs, J. V., and Sturgis, S. H., editors: *Progress in Gynecology*, ed. 2, New York, 1950, Grune and Stratton, p. 463.
23. Helseal, E. D.: *AM. J. OBST. & GYNEC.* 52: 435, 1946.
24. Bonini, L. D'I.: *Ann. ostet. e ginec.* 72: 761, 1950; *Internat. Abstr. Surg.* 92: 469, 1951.
25. Pemberton, Frank: *AM. J. OBST. & GYNEC.* 55: 201, 1948 (discussion).
26. Parks, T. J.: *AM. J. OBST. & GYNEC.* 49: 676, 1945.
27. Schumann, E. A.: *AM. J. OBST. & GYNEC.* 55: 201, 1948 (discussion).

Discussion

DR. LUDWIG A. EMGE, San Francisco, Calif.—Dr. Randall's analysis of the experience gained from treating ovarian cancer at the Buffalo General Hospital again testifies to our inability to cope successfully with this vicious killer. Twenty years ago I reported

that the five-year survival rate for ovarian cancer treated at the Stanford Women's Clinic was 19 per cent. Before the report came off the press two of the survivors had died quite unexpectedly from distant metastases which taught us that five years was not long enough to predict a cure. Since then our material has increased to 122 cases of primary adenocarcinoma of the ovary and some fifty other miscellaneous ovarian malignancies, each group having a different survival rate. The five-year survival rate for primary adenocarcinoma of the ovary treated by us in the Stanford Women's Clinic averaged 15 per cent, more or less, varying with each decade, sometimes encouragingly improved and then again distressingly depressed. The Buffalo group, therefore, need not be discouraged over a rate of 14.4 per cent. It differs little from the general experience and is bound to vary with time.

I am under the impression that private gynecologic patients seem to fare better because eleven of 43 patients afflicted with ovarian cancer treated by me prior to 1948 have survived from five to twenty years, an incidence of 25.5 per cent. Acknowledgedly, this sample is too small to warrant definitive statements, yet the figure is encouraging, though the explanation is not easy. Perhaps closer individual care, long experience, and surgical judgment are factors of importance although it is just as likely that education regarding the dangers of cancer is the really significant factor, because the surveys of large insurance companies which constantly propagandize the dangers of cancers, show a steady decline in the death rate of genital cancer among their female industrial policy holders. Private patients, definitely, are more aware of the need of periodic examination, hence the chance discovery of an early asymptomatic ovarian cancer is enhanced, which in turn naturally favors a better cure rate.

Dr. Randall made reference to the co-existence of granulosa-cell tumors and endometrial cancer which has been given particular significance by several investigators in attempting to link hyperestrinism with the etiology of uterine cancer. It has been pointed out by Hertig, Dockerty, and Novak that the percentage of the co-existing occurrence transcends figures which can be explained by chance alone (Hertig 18 to 20 per cent, Dockerty 16 per cent). Since 21 granulosa-cell tumors and 8 thecomas listed in our files were not accompanied by corpus cancer, and since hyperplasia of the endometrium was encountered in only 30 per cent of our patients I looked about for further information on the co-existence of uterine cancer and granulosa-cell tumors. Through the kindness and cooperation of a number of my acquaintances heading large clinics I obtained the following figures. Thirty clinics reported a total of 514 granulosa-cell tumors and the co-existence of 17 endometrial cancers, an incidence of 3.30 per cent. This incidence is far below the figures recorded by Hertig and by Dockerty. If the figures from the three other clinics reporting "no co-existence" were known I am certain that the incidence would have deteriorated further. It is not altogether presumptuous to say here also that if the cytology of the purported adenocarcinomas of the endometrium were to be reviewed, some of the previous diagnoses probably would be rejected as was done by Dr. Leon Motyloff who reviewed and rejected Grete Stohr's report (*AM. J. OBST. & GYNEC.* 43: 586) of the co-existence of the two tumor entities (personal communication). Dr. Motyloff wrote to me about an instance of adenocarcinoid of the endometrium with a granulosa-cell tumor which further illustrates this point. In this case the uterus was not removed until six weeks after the diagnosis of corpus cancer had been made. A study of the endometrium at that time revealed nothing but glandular hyperplasia. No doubt, there are other instances known where the uterus was preserved in spite of a questionable adenomatous pattern and where no cancer occurred subsequently. Such instances should be reported in order that we may learn more about the real meaning of the co-existence of granulosa-cell tumors and endometrial cancer. In passing, I like to call attention to the not infrequent co-existence of other ovarian neoplasms with adenocarcinoma of the uterus. Randall, Mirick, and Wieben (*AM. J. OBST. & GYNEC.* 61: 596, 1951) reported the co-existence of 9 benign ovarian tumors in 330 cases of endometrial cancer, or 2.7 per cent, 7 malignant ovarian tumors, or 2.1 per cent, and 5 feminizing tumors, or 1.5 per cent. I reviewed the histories of 116 consecutive private patients afflicted with endometrial cancer and found the incidence of co-existence to be 4.7 per cent for benign and 1.9 per cent for malignant ovarian neoplasms but none for feminizing tumors. Statistics are tricky tools and often misleading. One should always know the sample and the sampler before giving too much weight to percentage figures.

Among those reporting their experience with the co-existence of granulosa-cell tumors and endometrial adenocarcinoma some also listed the over-all number of corpus cancers seen during the same period. When I collected these figures the total came to 1,996 but there were only 7 cases of co-existing granulosa-cell tumors, or an incidence of 0.35 per cent. One could keep up this play with figures indefinitely and with the growth of the sample one would probably experience the steady deterioration of the incidence to the point of complete insignificance. However, there is a lesson in all this and that is that one must look at both sides of a controversial question before accepting either. As far as I am concerned, the occasional co-existence of granulosa-cell tumors with endometrial adenocarcinoma does not indicate by any stretch of imagination that estrogen imbalance is the cause of corpus cancer.

Whether or not to include so-called borderline cases of ovarian neoplasms in our survival statistics is a highly debatable procedure particularly since it often is next to impossible to arrive at an equitable interpretation of doubtful cytologic patterns. I suspect that the occasional report of unusually high survival rates for ovarian cancer is the result of leaning toward the radical side of interpreting borderline patterns for it seems hardly possible that survival rates twice and three times as high as the best recorded the world over could be explained on another basis. In order to get off the horns of this dilemma I have made it a rule to study the free liquid in ovarian cystic tumors for possible presence of free cancer cells. Their presence or absence makes the differential cytologic diagnosis of the pattern much more simple. I have also applied the same principle to prognosticating curability by collecting deposits of extracystic fluid so frequently encountered in the cul-de-sac of Douglas. The presence of free cancer cells in this fluid means that the disease has been disseminated regardless of the apparently intact capsule of the tumor. I have never seen a patient survive in spite of irradiation and radical surgery if free cancer cells were found in the cul-de-sac fluid.

Dr. Randall touched on the question of palliative treatment. I must confess as to serious doubt in my mind concerning our attitude toward treating patients by surgery or irradiation when there can be no doubt that the disease is progressing evidently toward a fatal outcome. It is natural for us to want to prolong life but it may not be in the best interest of those who, according to our present state of knowledge, certainly must die, and in my own experience will die a more agonizing death, physically and spiritually, when after palliative treatment the patient realizes the futility of the therapy. After thirty-five years of observation of the relative merits of palliative versus no therapy for widely disseminated ovarian cancer I have come to believe that patients with incurable disease will live just as long or longer and, surprisingly, with less misery and fear, and with less need for narcotics than the poor wretch who has been subjected to incomplete surgery or massive irradiation.

The value of the so-called prophylactic abdominal irradiation is difficult to measure. It calls for two operations but there is no doubt that it facilitates surgery where tumors have become adherent or where accessory circulation has become so extensive as to create an undue hazard. However, the procedure does not guarantee a cure although it retards the spread of the disease in isolated instances. Irradiation slows up the reformation of ascites provided that radiation therapy is undertaken after the abdominal cavity has been emptied of fluid, for it has been my experience that irradiation of ascitic abdomens, particularly if much distended, has no retarding effect. It certainly does not promote absorption of existing ascites.

Dr. Randall also mentioned the advisability of oophorectomy as a prophylactic measure in conjunction with hysterectomy. This, I believe, is wishful thinking and, to borrow Edward Schumann's classical remark, it is like cracking nuts with a sledge hammer, to which I add that it is an attempt to kill the problematic worm that probably is not there without smashing the meat of the nut. We know that untold numbers of women have lost their uteri for cause or no cause without developing cancer in residual ovaries. We also know that untold numbers have lost their ovaries because they are so easily removed or because the average operator knows so little about gross ovarian pathology, yet, pathologists do not raise their voices in protest where they find no ovarian pathology. It is commonly overlooked that the

woman afflicted with ovarian cancer rarely has had need for previous pelvic surgery. I reviewed the histories of forty-three private and forty clinic patients in this regard and found that only one patient had been subjected to surgery at the age of thirty. Again, this sample is too small but it serves to bring this subject to your attention. Perhaps you will verify it one way or the other on the basis of your own material. It might help immeasurably to correct the idea that the wanton removal of ovaries will materially reduce the incidence of ovarian cancer. I have heard it said by an otherwise serious gynecologist that the unilateral removal of an ovary would reduce the ovarian cancer incidence by 50 per cent. Not only is this silly biometrics but it is dangerous reasoning at a time when the trend is turning in favor of the preservation of ovaries.

Dr. Randall projected the predictable incidence of ovarian cancer in the aging female population as 3 in 1,000. That figure, I am certain, is too gloomy. Approximately 5,300 women (1948) die yearly from ovarian cancer and more may be expected to die as longevity increases, since the bulk of ovarian cancer falls into the sixth and seventh decades. With an average five-year salvage rate of only 15 to 20 per cent, which is probably too high for the population at large, and an adult female population of about fifty millions in this country, the incidence should more closely approximate 7 in 40,000. If it were otherwise, the average practitioner would see more ovarian cancer. It is my experience that many general practitioners have seen none or only so few that they hardly ever think of the possible presence of the disease. Here, also, a little more education would do no harm.

Dr. Randall's paper presents many other challenging topics I should have liked to discuss, particularly the occurrence of primary Krukenberg tumors with long survival periods, of which I have seen two instances, and the conservative surgical management of dysgerminoma, in the young, for I have several of these patients who have borne children and whose gratitude is eternal.

DR. HERBERT SCHMITZ, Chicago, Ill.—This is an excellent contribution to the subject of ovarian malignancies. I do not like to leave unanswered the pessimistic note which he has sounded. I feel that there is something we can do about the low survival rate in ovarian carcinoma. During a comparable period, 1935 to 1945, there were 143 patients with proved carcinomas of the ovary admitted to my service. Of this group, 113 had their primary treatment by me. All of the patients who were in an operable stage were subjected to surgical therapy, and those in an inoperable stage had colpotomy to obtain tissue for diagnosis.

TABLE I

CARDINAL SYMPTOM	NO. OF CASES	PER CENT
Abdominal swelling	65	45.4
Abdominal mass	28	19.6
Feeling of abdominal weight	9	6.3
Weight loss	19	14.0
Vaginal discharge	20	14.9
Urinary symptoms	9	6.3
Diarrhea, etc.	12	8.3
Menstrual irregularity	20	14.9
Not known	15	10.4
No symptoms	7	4.8

As is shown in Table I, there is no classical symptom, and the fact that vaginal discharge and menopausal bleeding is such a rare finding is, I believe, responsible for the fact that women consult the physician in the late stage of the disease. Forty-five per cent came because of abdominal swelling. Depending upon whether the woman had a cystic or solid tumor, this would indicate the presence of the neoplasm from three to twelve months.

The delay period was important. One month from the onset of symptoms only 23.7 per cent presented themselves. Too frequently because of absence of abnormal vaginal bleeding, which is the one symptom stressed by the American Cancer Society as indicative of genital cancer, these patients are quite smug and are sure that it must be some other situation. I am of the opinion that we must teach the laity that it is not sufficient to recognize abnormal bleed-

ing but that periodic examination, as advocated in the Hillsdale Plan, is necessary for protection against malignant disease. All patients should have a pelvic examination at least every six months.

TABLE II

LENGTH OF TIME	CASES	PER CENT
Under 1 month	34	23.7
Under 2 months	17	11.8
Under 3 months	8	5.5
Under 4 months	7	4.8
Under 5 months	6	4.1
Under 6 months	9	6.3
Between 6 and 9 months	1	0.07
Between 9 and 12 months	0	0.00
Between 1 and 2 years	10	6.9
Over 2 years	15	10.4
No signs	8	5.5
Not known	28	19.6

Eighty-one per cent of these patients were sent for therapy with a correct diagnosis within or under one month of the time they first reported to the physician. This, I believe, illustrates that the physician recognizes his responsibility and avoids physician delay. One hundred five of these patients were subjected to surgical procedure, which means total hysterectomy, bilateral salpingo-oophorectomy and the removal of the entire omentum. Too frequently patients have had an incomplete operation. When the microscopic diagnosis is returned, the physician realizes that he has been dealing with a malignancy and rather than confront the patient with reoperation, he procrastinates and advises radiation.

TABLE III

LENGTH OF TIME	CASES	PER CENT
Under 1 month	116	81.4
Under 2 months	15	10.4
Under 3 months	4	2.8
Under 6 months	4	2.8
Under 12 months	3	2.0
Under 2 years	1	0.07

Table IV gives us the survival rate for the entire series. If we eliminate in the final tabulation those individuals in whom only supportive therapy could be instituted because of disease advancement, 38 cases in all, we would have a corrected survival percentage of 27.5 per cent.

TABLE IV

GROUPING	TOTAL CASES	FIVE-YEAR SURVIVAL	PER CENT
Group I	40	11	27.5
Group II	26	9	34.6
Group III	13	5	20.0
Group IV	26	4	15.3
Group V	38	0	0.0
Total	143	29	20.3

Early presentation of the patients to the physician is going to be the solution in overcoming this deplorable survival rate that Dr. Randall reports.

DR. FRANK R. SMITH, New York, N. Y.—I cannot help but reiterate what Dr. Schmitz has said about trying to dispel any pessimistic note that has been made on cancer of the ovary. I think it depends so much on the type of tumor involved. I was most interested in Dr. Randall's presentation of his patients with dysgerminoma, and to find that practically

half of them had died. We have had 14 of them at the Memorial Hospital and none of these patients have died. They are the most radium-sensitive group that we have seen. Most of them have been operated upon and closed as hopeless at other hospitals, but these tumors melt away under adequate irradiation. We have one patient, now about eight years postirradiation, who had fluid in her chest associated with ascites when first seen by us. We treated her with x-ray. She is alive and has married, although she will not produce children because she has been sterilized by the treatment.

DR. THADDEUS L. MONTGOMERY, Philadelphia, Pa.—The excellent statistical analysis of end results in ovarian malignancy which has been presented by Dr. Randall emphasizes the fact that treatment of cancer in this area is the least satisfactory of that of any organ of the reproductive tract. The dictum which was used in the early part of World War II would certainly be applicable here, "too little, too late."

But the proposition of changing this pessimistic phrase to "enough, in time" is very difficult to envisage in the near future. The very nature of the lesion makes early diagnosis and early therapy unlikely; for unless by chance the lesion is detected before early rupture of the capsule disseminates carcinoma throughout the peritoneal cavity, a surgical cure is well nigh impossible.

For this reason it is unfair to ascribe poor results of therapy to the failure of the patient to consult a physician in sufficient time. Actually ovarian carcinoma may make its appearance, rupture the capsule, and become inoperable between two semiannual visits of a very faithful patient. And, in addition, the lesion usually has no significant subjective symptoms which would bring the patient to the gynecologist until widespread peritoneal metastasis and abdominal distention have occurred.

There is the difficulty in diagnosis even when the patient comes with a slight detectable enlargement of the ovary, for, in such instance, the physician is prone to advise the patient to return for a recheck in five or six weeks, in order to differentiate between a simple follicular cyst, a smooth-walled dermoid, and the more serious neoplasms of the ovaries. In the ensuing six or eight weeks, the rupture of the capsule of the ovary may take place, and dissemination of the lesion occur.

The crux of this whole situation is, naturally, early diagnosis, but thus far no one has provided a satisfactory solution of this very problem. It has been pointed out that periodic subsequent vaginal examinations may only permit the fatal extension of the lesion. It is doubtful that Papanicolaou smears from the cervix or from the posterior cul-de-sac of the peritoneum will prove of value in early diagnosis, for if they are positive, it simply means that the ovarian neoplasm has already thrown off malignant cells, and that implants must certainly have occurred in the peritoneum. Perhaps culdoscopy or even posterior colpotomy is indicated in all cases of ovarian enlargement, though there are physiological changes in the ovaries during the active sexual life of the individual, which confuse the picture, and would give rise to many unnecessary procedures of this type.

This problem of the early diagnosis of ovarian cancer has been coming up time and again before the Pelvic Cancer Committee of Philadelphia. Thus far, we have found no solution. I am sure that Dr. Randall has turned this matter over in his mind many times as he has reviewed and arranged these statistics. Perhaps he has a solution of the problem of diagnosis of ovarian malignancy before perforation.

DR. WM. E. STUDDIFORD, New York, N. Y.—I would like to report briefly a case which may cast some light on difficulties in early diagnosis in these very malignant cases of cancer of the ovary. A few years ago a colleague of mine operated on a patient who had fibroids at the age of 50 and hemorrhaged. Because of her age he performed a total hysterectomy and bilateral oophorectomy. There was nothing grossly in the ovaries to suggest anything abnormal at all. There was a free bloody fluid in the cul-de-sac. On microscopic examination there were three separate and distinct tumors on the right side. One of these tumors was a very malignant cancer of the ovary which had perforated the capsule and produced metastasis on the opposite side. Despite an exceedingly early removal, this patient was dead within a year and a half with general carcinomatosis of the abdomen.

DR. EMIL NOVAK, Baltimore, Md.—Dr. Schmitz tried to infuse a bit of optimism into this rather gloomy field of ovarian cancer, and Dr. Schmitz sounded a similarly optimistic note as to the prognosis with dysgerminoma. On the latter point our experience, as well as that offered by the material of the Ovarian Tumor Registry, has been definitely less favorable. Thus far, the recurrence rate of these tumors, which so many take so lightly, has been something like 30 to 32 per cent. Dr. Smith also mentioned the possibility of adenoma malignum and other forms of endometrial adenocarcinoma in association with granulosa-cell carcinoma or thecoma, and Ingram and I have recently collected 54 instances of this association. In this paper we called attention to the possibility of interpreting as adenocarcinoma certain atypical hyperplasias which are actually benign.

Many surgeons have had the unpleasant experience of getting a pathologic report of carcinoma several days after the unilateral removal of an ovarian tumor. The wisest procedure in most such cases, distressing though it is to both the patient and the surgeon, is to perform a radical operation. The tendency of ovarian malignancy is always toward bilaterality and even though the other ovary appeared normal at operation, it may already contain nests of cancer cells in the lymphatics of the medulla, as I found in the study of a group of such cases a good many years ago.

Finally, Brenner tumors have always been looked upon as clinically benign, and certainly this is the rule. In the past few years, however, several unquestionably malignant Brenner tumors have been reported by Dubraunsky and others.

DR. RANDALL (Closing).—I appreciate the discussion and interest, and certainly agree that we should have a question-and-answer period regarding ovarian malignancies. I would like to ask Dr. Novak if the Brenner tumors reported to be malignant could be malignancies developing in the cystomatous elements of an ovarian neoplasm also displaying Brenner characteristics. We have certainly observed instances in which a pseudomucinous cystoma and a smaller Brenner tumor arising in the same ovary both looked benign. Is it the characteristic Brenner picture alone in which malignancy seems to have developed?

I am not by nature a pessimist, but it is difficult for me not to be pessimistic about ovarian malignancies. We were particularly interested in a few cases in which carcinoma of the ovary was "discovered" at laparotomy, so early that no growth had apparently extended through the capsule. However, in only two of five such cases, the patient survived five plus years. While so small a series does not justify conclusions, in answer to Dr. Montgomery's question, "How can we identify ovarian cancer?" this experience suggests that we cannot do so by palpation or on routine pelvic examination. At least we probably could not distinguish between benign neoplasms of the ovary and malignancies so early that the capsule appeared intact without perforation, implantation, or adhesions.

I have no experience on which to evaluate culdoscopy and I do believe that exploratory laparotomy is indicated any time the ovary seems enlarged after the menopause. Even so, at the present time I see no possibility of appreciably decreasing the number of deaths due to ovarian malignancy unless we remove normal ovaries before they become involved. Since it does not seem to me that the actual incidence of ovarian malignancies justifies such prophylactic oophorectomy, this review leaves me pessimistic about ovarian carcinoma at the present time.

ENDOMETRIOSIS IN PREGNANCY, CLINICAL OBSERVATIONS*

HAROLD L. GAINNEY, M.D., JAMES E. KEELER, M.D., AND
KENNETH S. NICOLAY, M.D., KANSAS CITY, MO.

THIS discussion of endometriosis associated with pregnancy is restricted to external endometriosis. The exclusion of internal endometriosis is based on concurrence in the belief that the two diseases are etiologically separate and their relationship to pregnancy distinctly different.

The literature to date suggests that endometriosis associated with pregnancy is infrequent. Articles dealing with the subject specifically are few. The already voluminous and rapidly increasing literature regarding endometriosis deals with etiology, pathogenesis, and management, medical or surgical. Discussions pertinent to endometriosis associated with pregnancy are involved with review of literature with additions of case reports. Scott¹ did service in this respect and subsequently scattered case reports have been recorded. The initial appearance of this subject in a standard textbook was made in 1950.²

It has been stated that "combining a discussion of endometriosis and pregnancy is in some measure a paradox." This is further supported by the belief that the lesions are associated with infertility, relative and absolute. There are many comments in the abstract bearing upon the effect of the one on the other. These opinions vary in extremes. Goodall,³ in 1943, stated that in his experience with hundreds of cases of endometriosis he had never seen pregnancy and, further, that it was fortunate the two conditions never coexist. Meigs,⁴ originally in 1922, and two years later Sampson,⁵ put forth the supposition that the lesion might be favorably influenced by pregnancy. Beecham,⁶ in 1949, said, "Nature (since the beginning of time) has employed an efficient prophylactic and curative measure for endometriosis, i.e., pregnancy." In the same discussion he said, "Pregnancy must be considered the ultimate in endocrine therapy, but why the physiologic amenorrhea causes the endometrial implants to regress, we do not know." Randall,⁷ in the same year, discussing therapeutic effects of estrogens, said, "Foci of endometriosis seem to improve remarkably during pregnancy." These authors did not offer substantiative evidence for these statements, yet I am sure it must be available.

The recommendation to the endometriosis victim to conceive is repeatedly observed in the literature, but whether for its therapeutic effect or in anticipation of associated infertility, is not too clear. This latter concept was productive of cases for this report.

Material

The 38 cases presented here represent a selected group of patients with endometriosis in pregnancy and are of two categories, with respect to observation: One, those in which histopathologic evidence confirms or lends support; and the other, those in which only physical findings substantiated the diagnosis.

*Presented at the Sixty-second Annual Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 6, 7, and 8, 1951.

It is important to note that, in both categories, a positive diagnosis is oftentimes difficult. In the first category, there were 13 confirmed by histologic study, 7 during pregnancy and 6 prior to the pregnancy or pregnancies observed. In the second category, 25 were considered to have had the diagnosis established by multiple examining gynecologists, in some as many as 4; by repeated examinations, from 4 to 40, or slightly over 9 per patient; and by observation over prolonged periods of time, the shortest three months and the longest 11 years, with an average of three years. A constant factor has been the examination of all patients by one of the authors (H. L. G.).

The use of culdoscopy has been avoided in these patients.

The histologic diagnosis with absolute finality in ectopic endometrial tissue is oftentimes obscured by difficulty in establishing proof and identity of the presence of epithelial elements in the decidual structures. The natural evolution of the endometrium, uterine or ectopic, in various stages of pregnancy demonstrates the change of the glandular epithelium from its typical columnar papillary secretory cells to flat, slitlike spaces lined only with low cuboidal to flat mesothelial or endothelium-like structures. The capacity of the germinal epithelium of the ovary and the mesothelial cells of the peritoneum to undergo changes resembling glandular structures is well known. Tissue differential stains were of no assistance.

The authors were impressed with the specificity of decidual tissue and if careful search was made adenomatous tissue could be found in the majority of instances. This impression is supported by observations of de Jong and de Snoo⁸ that most of the ectopic decidual nodules observed during pregnancy on the peritoneum and ovaries are foci of endometriosis which have undergone degenerative changes during pregnancy, and⁹ that decidual nodules in the pelvis bear the same numerical incidence and anatomical distribution as ectopic endometrium in the nonpregnant. This is offered in spite of the observation of the presence of decidual-cell accumulations in from 25 to 30 per cent of ovaries observed at term laparotomy. The prediction of uniform behavior of ectopic endometrial tissue is not possible histologically in pregnancy, and the theoretical explanations offer the source of the "implants" as an explanation. Novak and de Lima¹⁰ said, "The aberrant endometrium of both adenomyosis and endometriosis is usually of an immature variety, its immaturity being evidenced by the fact that it is physiologically responsive only to the growth stimulus of estrogen, and not to the differentiating influence of progesterone. There are, of course, some exceptions, the exact incidence of which it is difficult to set down with accuracy." Martzloff¹¹ elaborates the feature that in some patients the ectopic endometrium is of the so-called basal type and not responsive to ovarian stimulation. Faulkner and Douglas¹² state that, "True endometrial implants with stroma undergo decidual reaction wherever they are." They explain variation in response by the origin of the ectopic tissue, that which arises as a result of metaplasia being immature endometrium and nonfunctional. These lesions are likely to have little if any surrounding stroma. They further postulate that older implants in which the epithelium has been partly destroyed by repeated cyclic response and menstruation are less likely to show response to hormonal stimulus.

In the light of these concepts, there should be no constant characteristic response, clinically or histologically, of this disease to the hormonal changes of pregnancy. The anticipated reaction in a given pregnancy would be determined by the origin of the ectopic tissue, the age of the ectopic implants, and the amount of stroma in any given lesion.

Recorded statements of difficulty with suitable animals (*Macacus rhesus*) for studies of this type make observations of clinical nature mandatory. Accordingly Te Linde and Scott¹³ stated, "It behooves the gynecologist to uncover

more fundamental information in order that the disease be prevented or more adequately treated." The combined specialty of obstetrics and gynecology is admirably suited to this end.

The authors of this paper reluctantly, but with a degree of confidence, present a group of clinically observed patients. The increase in the accuracy of clinical diagnosis generally is considered partially responsible for the increased incidence of the disease. Few authors quote incidence of the disease, obviously hesitant to offer material not substantiated by histologic confirmation. The recent enthusiasm for evaluation of hormonal therapy with published reports implies acceptance. Jenkinson and Brown¹⁴ give an incidence of 15 per cent; Beecham,⁶ 5.8 per cent; Siegler and Bisaccio¹⁵ 8 per cent; and ours of 5.2 per cent in gynecological patients is compatible.

In substantiation of the rationale of presenting clinically observed cases, we quote from Pratt,¹⁶ "I quite agree that there are many more cases of endometriosis and pregnancy than have been reported and it is a great deal more common than we know." He further stated, "Reports in the literature are based too much on the findings of the condition at operation."

The cases observed for report here have been drawn from 8,300 private obstetrical and gynecological patients, of whom 2,780 were admitted as obstetrical patients who subsequently delivered 3,540 term infants. The incidence of endometriosis in both obstetrical and gynecological patients was 3.4 per cent, 5.2 per cent in gynecologic patients, and a 1.4 per cent incidence of endometriosis associated with pregnancy.

The age incidence in patients with endometriosis in pregnancy ranged from 21 years in the youngest, to 38 in the oldest, with an average of 29 years.

Fertility data are discussed in view of the time without intervening pregnancies and so of uninterrupted menstruation, rather than of infertility, as detailed knowledge of the contraceptive practices is incomplete. The average interval married and without or since last pregnancy was 3.8 years. Only 5 patients presented themselves primarily as sterility problems, while 2 others gave sterility as a secondary complaint. Seventeen, or 47.4 per cent were pregnant when first seen.

Location of Lesions

The following areas were observed in regard to frequency: Uterosacral ligament, 20, or 52.5 per cent; ovary 2, or 5.3 per cent; combined uterosacral ligament and ovary 14, or 37.0 per cent; rectovaginal and cervix 1 each, or 2.6 per cent each.

TABLE I. LOCATION OF LESIONS

LOCATION	NUMBER	PER CENT
Uterosacral ligament	20	52.5
Ovary	2	5.3
Uterosacral ligament and ovary	14	37.0
Rectovaginal	1	2.6
Cervix	1	2.6
Total	38	100.0

Observations

The effect of pregnancy on the lesions was recorded subjectively and objectively. Thirty-four patients were in this group.

Objectively 14, or 41.2 per cent of this group, showed improvement in pelvic findings following pregnancy. Twenty, or 58.8 per cent, revealed no change. In the ones showing no improvement this was true following one or

more pregnancies, with one exception. Case 13 showed no improvement following her first pregnancy, but did show improvement following the second.

Twenty-five patients were eligible for discussion under the heading subjective complaints, 9 having no symptoms referable to endometriosis, infertility not considered. It was recorded that 20 of the 25, or 80.0 per cent, noted subjective improvement, varying from improvement to disappearance of associated complaints. Three patients with uterosacral ligament, and 2 with uterosacral ligament and ovarian endometriosis reported no improvement as evaluated from antenatal to postpartum questioning.

The most striking improvement was in Case 12, with extensive rectovaginal involvement where almost total involution, beginning in the last part of the second trimester, persisted to the last examination eight months post partum, in the absence of nursing and in the presence of resumption of menses.

TABLE II. POSTPARTUM OBSERVATIONS

LOCATION	NUMBER	IMPROVED		UNIMPROVED		RECURRENCE TIME INTERVAL POSTPARTUM
		OBJEC- TIVELY	SUBJEC- TIVELY*	OBJEC- TIVELY	SUBJEC- TIVELY*	
Uterosacral ligament	20	8	11	12	3	1 (1 year)
Ovary	1		1	1		
Ovary and uterosacral ligament	12	5	7	7	2	(2 years)
Rectovaginal	1	1	1			2 (4 years)
Total	34	14	20	20	5	

*Nine patients had no subjective complaints referable to endometriosis.

It is of interest to note that recurrence was recorded in 3 patients, at four years, two years, and one year, respectively.

A most significant finding was that in no case did examination in the puerperium reveal stimulation or increase in the lesions as a result of pregnancy.

A group of 4 cases is discussed with respect to their relationship to pregnancy, because surgical intervention interrupted or altered the lesions in a manner making group analysis inaccurate.

One patient (Case 38) had torsion of the right adnexa in the second trimester of pregnancy with surgical removal of the affected ovary in which a diagnosis of endometrioma of the ovary with decidual reaction was made.

Two patients were operated upon with preoperative diagnosis of ectopic gestation; in one (Case 35), there was a primary ovarian pregnancy with extensive cul-de-sac and uterosacral ligament endometriosis, and the other (Case 36) had a rapidly enlarging endometrial cyst of the left ovary associated with an intrauterine gestation of four weeks' duration.

One patient (Case 37) had a rapidly growing lesion, anteriorly, on the vaginal portion of the cervix which was excised at ten weeks' gestation. Histologic diagnosis revealed an endometrioma of the cervix with decidual reaction.

The constant histologic finding was one of decidual reaction with epithelial elements varying from glandular structures lined with tall columnar secretory cells in those associated with early pregnancy (cervical and ovarian lesions), to low cuboidal and flat endothelium-like epithelium in late and term pregnancy (Cases 7, 9, and 32). These findings were comparable to uterine decidua obtained from pathologic material in the laboratory from surgical and necropsy specimens. They were of as early as four weeks' to term gestation, the latter a necropsy specimen from a term intraligamentous pregnancy.

Histologically, there was no explanation found for the involution of these lesions as recorded clinically in 3 cases seen in the latter "half" of pregnancy

and persistent in the late puerperium; Case 12, eight months, Case 7, four years, and Case 9, four years. These were one each rectovaginal, uterosacral ligament, and ovarian endometriosis.

The description of the postpartum cellular degenerative changes in the ectopic tubal decidua reported by Milnor and Tilden¹⁷ were not observed, but it must be noted that none were studied histologically during the "regression phenomena" or post partum in either the cases reported or in the control uteri.

Complications

Review of the literature suggests that endometriosis and pregnancy may coexist without untoward consequences. Our experience parallels this observation with few exceptions, as do occasional case reports from the literature.

In this series, 46 children were delivered following the diagnosis of endometriosis. There were 6 abortions in 57 pregnancies, or 10.5 per cent (5 undelivered at the time of this report). In a control series of 1,000 obstetrical patients, the incidence of abortion was 9.5 per cent.

Two complications of pregnancy could not be readily separated from endometriosis; the torsion of adnexa with ovarian cystoma of endometrial origin is inseparable, and the likelihood of endometriosis providing a nidus for the primary ovarian pregnancy is at least a probability. Placenta previa and the postpartum convulsive toxemia were considered unrelated.

TABLE III. COMPLICATIONS OF PREGNANCY

Number of patients		38
Number of pregnancies		57
COMPLICATION		NUMBER
Torsion of adnexa on one side		1
Ovarian pregnancy		1
Abortion		6
Threatened abortion		1
Placenta previa		1
Toxemia, postpartum, convulsive		1

The 4 cesarean sections (Cases 7, 9, and 32) were done for primarily obstetrical indications and in no way related to endometriosis. This same conclusion was drawn in the other complications of parturition: prolonged labor 2, postpartum hemorrhage 4, and premature delivery 4. These complications occurred in 11 patients.

TABLE IV. COMPLICATIONS OF LABOR

Number of patients		34
Number of deliveries		46
COMPLICATION		NUMBER
Cesarean section		4
Postpartum hemorrhage (over 350 c.c.)		4
Prolonged labor (over 24 hours)		2
Premature delivery		4

Case Reports

CASE 7.—(Pathology No. 48-5556) A 34-year-old white woman, gravida 0, para 0, married five years, was first seen in 1946 with the complaint of left lower quadrant pain. She gave the history of previous (1943) right salpingo-oophorectomy with the diagnosis of endometriosis. Pelvic examination revealed a large left adnexal mass, clinical diag-

nosis ovarian and uterosacral ligament endometriosis. Surgery was recommended but amenorrhea followed. Diagnosis of pregnancy was made. By the fifth month, the mass had disappeared and the only evidence of endometriosis was scarring in the uterosacral ligaments. At term, there was premature rupture of the membranes with a floating presenting part. Because of her age (35 years), infertility, absence of adnexa on one side and disease on the other, an elective cesarean section was performed. At laparotomy, the left tube was found to be patent but distorted by thin, broad, adhesive, avascular bands. The ovary was two-thirds normal size and fixed to the posterior leaf of the broad ligament. Postpartum examination revealed marked improvement in the pelvic findings. She became pregnant one year later and had a repeat cesarean section at term, with the same pelvic findings. Biopsy at this time confirmed the diagnosis of endometriosis (Fig. 1). At six months and two years post partum the left ovary was again enlarged and fixed, though not as markedly enlarged as prior to pregnancy. At three years post partum there had been spontaneous remission with only minimal uterosacral ligament pathology noted.

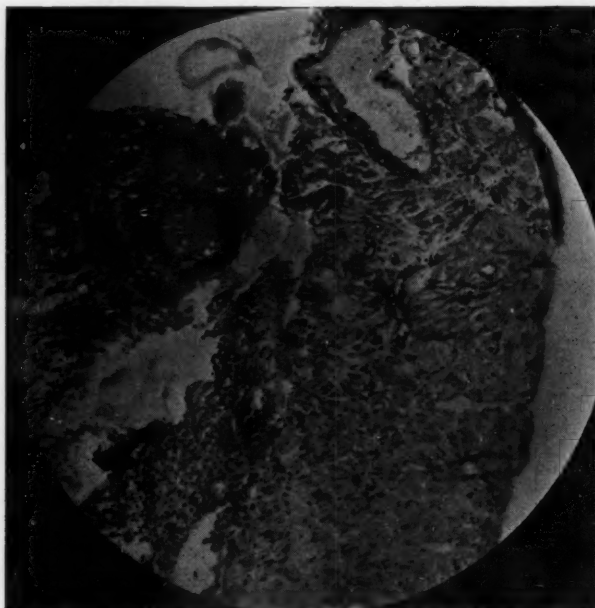


Fig. 1.

Fig. 1.—(Case 7).—Section of ovary showing decidual reaction and gland lined by flat epithelial cells.

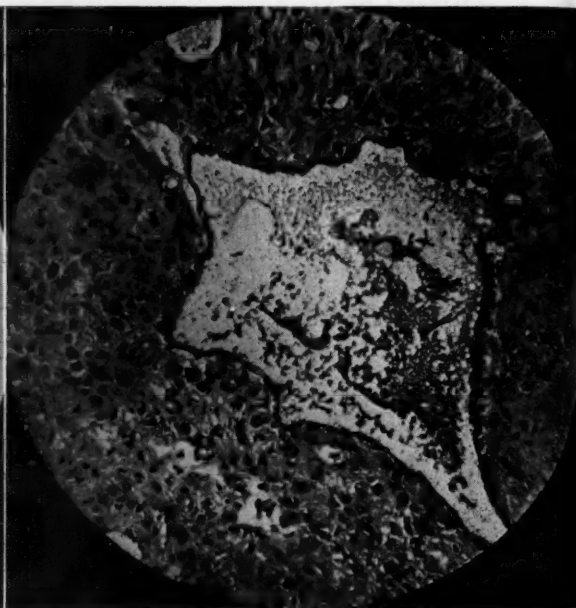


Fig. 2.

Fig. 2 (Case 9).—Section of uterosacral ligament showing ectopic endometrial gland and decidual reaction.

CASE 9.—(Pathology No. 47-2128) A 38-year-old white woman, gravida ii, para i, married five years, with a 3-year-old child, was first seen at ten weeks' gestation. Previous pregnancy terminated by cesarean section elsewhere with indications unknown. Pelvic examination revealed extensive induration of the uterosacral ligaments and bases of the broad ligaments. Near term, there were softening and almost disappearance of the induration. There were no interval examinations. A repeat cesarean section was done at term and biopsy of the uterosacral ligaments confirmed the diagnosis. Histologic diagnosis was endometriosis of the uterosacral ligament with decidual reaction (Fig. 2). Immediate and follow-up examinations for four years reveal no evidence of endometriosis.

CASE 12.—(Pathology No. 46-2592) A 31-year-old white woman, gravida 0, para 0, married three years, was first seen in 1946 with a diagnosis of endometriosis of the ovary, uterosacral ligament, and cul-de-sac. A left oophorectomy and suspension were done.

Four months postoperatively perforating rectovaginal lesions were noted. The findings remained unchanged until 1950. There had been minor exacerbations and remissions in pelvic findings without treatment. Last menstrual period was Jan. 9, 1950. Early, there was increase in the size of the vaginal lesion with later regression. By the twenty-fourth week of gestation there was no evidence (on examination) of endometriosis anywhere in the pelvis. There was a full-term, uncomplicated delivery. Examination at eight months post partum revealed only a very small puckered scar in the posterior fornix of the vagina. The patient had always been asymptomatic except for infertility and remained so post partum.

CASE 32.—(Pathology No. 51-3972) A 28-year-old white woman, gravida ii, para i, married four years, with a 2-year-old child, was first seen at thirty weeks' gestation in her second pregnancy. A diagnosis of endometriosis of the uterosacral ligament was made at that time. At thirty-four weeks' gestation, she developed massive, painless bleeding. Pre-operative diagnosis of placenta previa was confirmed at cesarean section. Both uterosacral ligaments were found distorted in their proximal portions by nodular infiltrative lesions. The color was grayish pink. Biopsies were taken. Histologic diagnosis was endometriosis of the uterosacral ligaments with decidual reaction (Fig. 3). At the time of this report the patient is only four weeks post partum and there have been no examinations.



Fig. 3 (Case 32).—Section of uterosacral ligament showing glandular epithelium with decidual reaction.

CASE 35.—(Pathology No. 50-1316) A 38-year-old white woman, gravida iv, para ii, with the youngest child 9 years of age, when first seen, was examined and a diagnosis of extensive endometriosis of the cul-de-sac was made. One year later she was seen seventeen days past her last "normal" menstrual period with persistent, severe, right lower quadrant pain of twelve days' duration. She presented evidence of intra-abdominal bleeding. The Friedman test was negative. Preoperative diagnosis was made of ectopic gestation. Diagnosis at laparotomy was primary ovarian pregnancy. A right oophorectomy was performed and a diagnosis of pelvic endometriosis was confirmed. The pathologic diagnosis was primary ovarian pregnancy, showing extensive decidual reaction (Fig. 4). Follow-up examinations revealed persistence of lesions, unchanged.

Fig. 4.

Fig. 5.

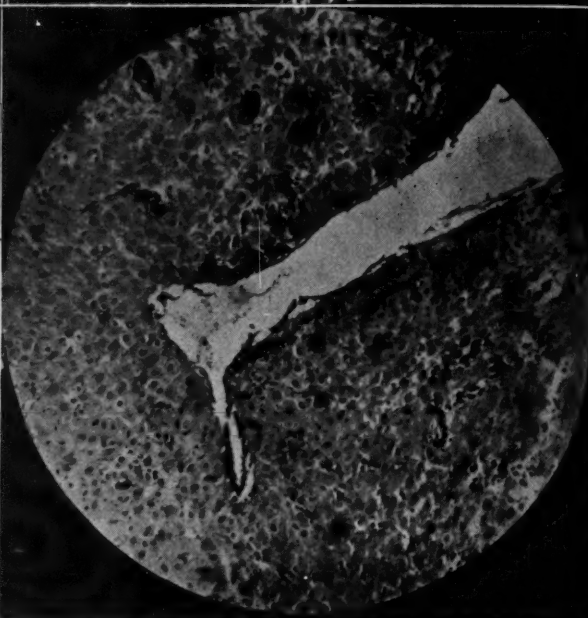
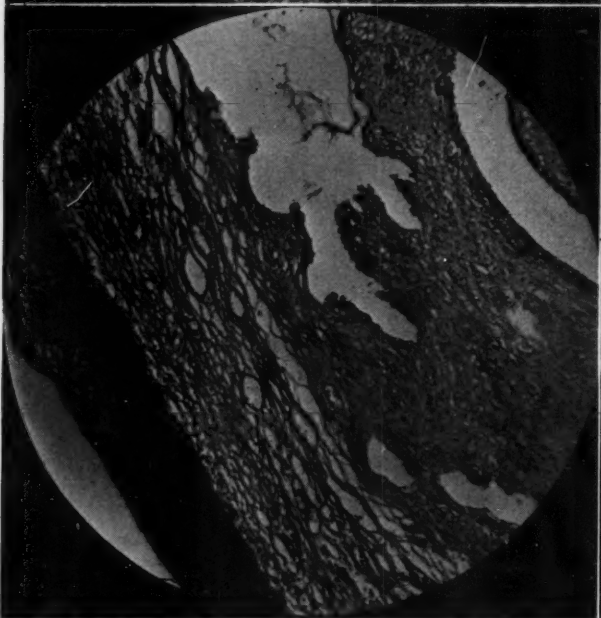
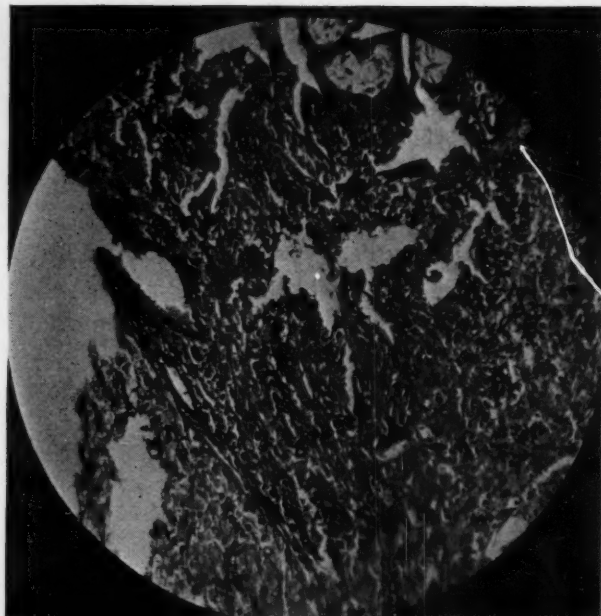


Fig. 6.

Fig. 7.

Fig. 4 (Case 35).—Section of ovary showing fetal villi and decidua on right side.
Fig. 5 (Case 36).—Section of ovary showing ectopic endometrial gland and decidua reaction.

Fig. 6 (Case 37).—Section of cervix showing squamous epithelium on left, decidua reaction on right, with glands of ectopic endometriosis and cervical connective tissue stroma between the two areas.

Fig. 7 (Case 38).—Section of ovary showing decidua reaction and gland lined by epithelium of endometrial origin.

CASE 36.—(Pathology No. 50-5774) A 37-year-old white woman, gravida ii, para i, married sixteen years, with a 14-year-old child, was first seen five weeks past her last menstrual period with complaints of sharp pain in the lower abdomen of two weeks' duration, becoming more severe. Pelvic examination revealed a retrodisplaced uterus with bilateral, fixed adnexal masses, 6 cm. on the right and 3 cm. on the left. Both uterosacral ligaments were extensively infiltrated with tender nodules. Diagnosis was made of ovarian and uterosacral ligament endometriosis in association with ectopic gestation. Over a period of seven days' observation in the hospital the left mass enlarged rapidly, the pain increased, and the Friedman test was positive. A diagnosis of tubal pregnancy was made. Laparotomy revealed an early intrauterine gestation with cystoma of the left ovary, 8 cm. in diameter, which ruptured at the time of removal, spilling contents of typical chocolate color. The right ovary was 3 to 4 cm. in diameter, fixed in association with typical endometriosis of the broad and uterosacral ligaments. Histologic diagnosis: endometriosis of ovary (Fig. 5). Two weeks following surgery the patient aborted. Examination later revealed persistence of endometriosis. She has again conceived and is now pregnant with the lesions unchanged.

CASE 37.—(Pathology No. 50-4307) A 24-year-old white woman, gravida i, para 0, married five months, was first seen at six weeks' gestation. There was a small, elevated lesion on the vaginal portion of the anterior cervix, 5 mm. in diameter. During the following three weeks this lesion rapidly increased in size to 1.5 cm. in diameter and 1 cm. in height. Excision biopsy was done and the pathologic report was endometriosis of the cervix with decidual reaction (Fig. 6). The patient had an uncomplicated full-term delivery at forty weeks. No other evidence of endometriosis has been found on this patient on post partum examinations. There is no history of cervical trauma.

CASE 38.—(Pathology No. 49-3432) A 29-year-old white woman, gravida i, para 0, married three and one-half years, was first seen at twelve weeks' gestation. There was a 4 cm. ovarian mass in the right adnexa. This persisted unchanged. At twenty-four weeks, there was right lower abdominal pain which persisted, gradually becoming worse. There was acute exacerbation of pain four hours prior to surgery. The preoperative diagnosis was twisted ovarian cyst. At laparotomy the right tube and uteroovarian ligament had undergone counterclockwise torsion and characteristic discoloration. The ovary was the site of a 5 cm. cyst. The tube was restored to normal relationship and the color was immediately restored to normal. The ovary alone was removed. Exploration failed to reveal any other evidence of endometriosis. Histologic diagnosis was endometriosis of the ovary with decidual reaction (Fig. 7). The patient had an uncomplicated full-term delivery at forty weeks. No other evidence of endometriosis has been found during a follow-up of two years to date.

Comment

The postpartum examination of 34 patients with endometriosis having completed term pregnancies revealed objective improvement, by examination, in 14, or 41.2 per cent. Twenty, or 58.8 per cent revealed no change.

Three patients, one each with ovarian, rectovaginal, and uterosacral ligament endometriosis, revealed almost total involution of what, prenatally, were extensive lesions. This effect was persistent post partum for eight months in the rectovaginal lesion and four years in the other two.

In 25 patients, where subjective complaints could be attributed to endometriosis, improvement was noted in 80.0 per cent. It is impossible to assess all of the benefits to the effect of pregnancy on the endometriosis when recognition of the anatomical and functional changes that persist in the parous individual are considered.

It is significant to note that, as recorded post partum, no patient was worse, subjectively or objectively, as a result of the effect of pregnancy on pre-existing endometriosis, the rare complication excepted.

We wish to express our thanks to Ferdinand C. Helwig, M.D., Chief of Pathology, St. Luke's Hospital, Kansas City, Missouri.

References

1. Scott, Roger B.: *AM. J. OBST. & GYNEC.* 47: 608, 1944.
2. Eastman, Nicholson J.: *Williams Obstetrics*, ed. 10, New York, 1950, Appleton-Century-Crofts, Inc.
3. Goodall, James R.: *A Study of Endometriosis*, Philadelphia, 1943, J. B. Lippincott Company.
4. Meigs, J. V.: *Boston M. & S. J.* 187: 1, 1922.
5. Sampson, John A.: *Surg., Gynec. & Obst.* 38: 287, 1924.
6. Beecham, Clayton T.: *J. A. M. A.* 139: 971, 1949.
7. Randall, C. L.: *J. A. M. A.* 139: 972, 1949.
8. De Josselin de Jong, R., and de Snoo: *Virchows Arch. f. path. Anat.* 257: 23, 1925. Cited by Scott.¹
9. Weller, Carl V.: *Am. J. Path.* 11: 287, 1935.
10. Novak, Emil, and de Lima, O. Alves: *AM. J. OBST. & GYNEC.* 56: 634, 1948.
11. Martzloff, Karl: Discussion of Ware, H. Hudnall: *AM. J. OBST. & GYNEC.* 59: 715, 1950.
12. Faulkner, Robert L., and Douglas, Marion: *Essentials of Obstetrical and Gynecological Pathology*, ed. 2, St. Louis, 1949, The C. V. Mosby Company.
13. Te Linde, Richard W., and Scott, Roger B.: *AM. J. OBST. & GYNEC.* 60: 1147, 1950.
14. Jenkinson, E. L., and Brown, W. H.: *J. A. M. A.* 122: 349, 1943.
15. Siegler, Samuel L., and Bisaccio, Joseph B.: *AM. J. OBST. & GYNEC.* 61: 99, 1951.
16. Pratt, Jean P.: Discussion of Ware H. Hudnall: *AM. J. OBST. & GYNEC.* 59: 715, 1950.
17. Milnor, G. C., and Tilden, I. L.: *AM. J. OBST. & GYNEC.* 44: 324, 1942.

Discussion

DR. HOUSTON S. EVERETT, Baltimore, Md.—The paper which Dr. Gainey has presented serves a useful purpose in keeping before us the fact that the presence of endometriosis is not necessarily incompatible with normal pregnancy and delivery. He has mentioned several earlier reports which have indicated such an incompatibility, but his paper as well as several others, among which may be mentioned those of Scott and Te Linde, 1947, and Ware, 1949, have definitely demonstrated that the two conditions may occur simultaneously.

There are several points in Dr. Gainey's paper which have aroused in me a certain speculative interest. In the earlier part of his paper he has discussed the matter of decidual reaction in ectopic endometrium, and referred to the fact that several eminent authorities have claimed that in many instances the endometrium in endometriosis is not capable of normal response to the stimulation of ovarian hormones. This to me seems entirely contrary to the clinical phenomena encountered in endometriosis. The conclusion that such endometrium is incapable of normal response to stimulation by ovarian hormones drawn from histological study to my mind is of little value, since the endometrium so studied is most often distorted and transformed by compression from the distention of the cyst by accumulated blood. A similar distortion occurs in the uterine mucosa in cases of hematometra resulting from cervical stenosis, but one would not conclude from this that this normally placed endometrium is incapable of response to ovarian cyclical stimulation.

I believe, then, that any endometrium, no matter where located, is very likely to undergo decidual reaction under the influence of pregnancy. Not only is ectopic endometrium capable of such transformation, but the same is true of any Müllerian tissue, as demonstrated by the decidual reaction in tubal mucosa in cases of tubal pregnancy. As a matter of fact tubal mucosa undergoes just as definite, though not as striking, cyclical changes under the influence of ovarian hormonal stimulation as does the endometrium,

a fact which Novak and I demonstrated in 1928. Furthermore, tubal mucosa is at times capable of transformation into typical endometrium, as demonstrated in at least two papers by Sampson, one on postsalpingectomy endometriosis and his very last paper on endometriosis arising from tubal fimbriae. I published a paper along the same line in 1931 called, "Probable Tubal Origin of Endometriosis."

That endometriosis frequently results in infertility, however, cannot be denied. As the tubes in such cases usually grossly appear patent, the cause of such infertility has been a matter of speculation. The following case may be somewhat suggestive in this regard, and is also interesting in that it is similar to Dr. Gainey's Case 36. Unfortunately the diagnosis of endometriosis has never been made histologically, but all clinical evidence is very suggestive of that condition.

The patient first consulted me on Jan. 31, 1944, at the age of 26 years, because of sterility. She had been married three years, and had practiced contraception for only the first year. The menses had begun at age 13, but the interval had always been prolonged, six to eight weeks, with duration of seven days and rather severe dysmenorrhea. Examination revealed an apparently normal uterus but both ovaries were adherent posteriorly to the broad ligaments. Two Rubin tests on Feb. 25 and April 30, 1944, succeeded in forcing gas through the tubes only at very high pressures, the readings being 190/160 mm. Hg and 200/90 mm. Hg, respectively. The endometrial biopsies on both these occasions showed nonsecretory endometrium. In spite of these unfavorable findings, the patient became pregnant early in 1946, and was delivered normally at term on Oct. 23, 1946. During the first two months of the pregnancy the right ovary enlarged more rapidly than the uterus, reaching the level of McBurney's point. Subsequent to this it began to recede, and by the end of the fourth month was no longer detectable as abnormal in size.

On Jan. 28 and Dec. 2, 1947, the uterus was found to be normal, but the ovaries were still adherent and the right one about twice normal in size and cystic. A second normal pregnancy terminated normally early in April, 1949. No enlargement of the ovary was detected during this pregnancy, and on June 24, 1949, pelvic examination revealed essentially normal findings. Neither ovary any longer felt either adherent or enlarged.

Speculatively the infertility in this case could have been due either to narrowing of the tubal lumen as a result of kinking from peritubal adhesions, or to failure of ovulation resulting from periovarian adhesions. One wonders if the periovarian adhesions might have caused the menstrual irregularity, but this seems unlikely as such irregularity had been present from the very beginning of menstruation.

A second case demonstrated the possibility of pregnancy after conservative surgery for extensive endometriosis. This patient aged 28 years, married five years and never pregnant, was operated upon on Dec. 12, 1944. There was a large endometrial cyst 8 cm. in diameter densely adherent to the tube on the left side, and a smaller one 3 cm. in diameter on the right. The left tube and ovary were removed, and the cyst was resected from the right ovary. The patient has subsequently had two normal pregnancies, the last delivery having been in June, 1950. Examination Oct. 17, 1950, revealed pelvic organs which seemed essentially normal except for the absence of the left adnexa.

The patient was one of those included statistically in the paper of Scott and Te Linde, who reported 38 pregnancies occurring in 26 of 64 women who had had conservative operations with the preservation of the anatomical possibility of pregnancy, and who were married and desired children. The cases cited and such reports as those of Dr. Gainey, Ware, and Scott and Te Linde should deter us from ever despairing of the possibility of pregnancy merely because a woman is afflicted with endometriosis.

DR. E. LEE DORSETT, St. Louis, Mo.—Dr. Gainey and his co-authors had made an additional contribution to the yet not completely solved problem of endometriosis but by their painstaking work they have gone one step further forward than the other investigators and have added one phase of the subject that has not been dealt with except by a very few authors, namely, endometriosis in pregnancy.

Beginning with Sampson and with the additional work of Te Linde and Scott, this subject has been as well covered as possible but still there is much to learn and the disease is not easily diagnosed and is more often found by accident than being diagnosed prior to operation. The preoperative diagnosis is sometimes suspected more often than absolutely diagnosed. Of course, there are those cases in which a positive diagnosis can be made but many cases are overlooked due to a too hasty examination and snap diagnosis. There is no question that it is sometimes difficult if not impossible to make a diagnosis and this is true in conjunction with a pregnancy. It has been felt by many of us that endometriosis did not develop during pregnancy or if it were present before pregnancy and the woman became pregnant the disease would either subside or disappear. Of late this theory has to some extent been exploded.

I was very much surprised by the number of cases reported by Dr. Gainey but I am sure this is due to the care and time consumed in the examination and working-up of his cases and by the repeated examinations before and during pregnancy. Pregnancy has the bad habit of masking many pathologic conditions and it is only when these conditions become exaggerated and cause rather severe symptoms that they manifest themselves.

Injecting a personal element into this discussion, I hope you will bear with me while I briefly present the histories of two of my cases in which endometriosis was found in pregnancy; one undiagnosed and one unsuspected.

CASE 1.—The patient, aged 27 years, had always had dysmenorrhea, no previous pregnancies. At the beginning of this pregnancy she had rather unusual lower abdominal pain and when she was ten weeks pregnant there was present a pelvic tumor about 6 by 4 by 4 cm. in the cul-de-sac that had displaced the pregnant uterus to the right side of the pelvis. As this tumor caused the patient considerable pain a laparotomy was performed with a preliminary diagnosis of an endometrial cyst. The cyst was removed without disturbing the pregnancy and the patient went to term and was delivered. The pathological report was as follows: "The cyst wall showed that it was composed of endometrial like glands in a round and spindle cell stroma. The stroma cells showed a decidual change." *Diagnosis*, "Endometrial cyst of the ovary with decidual reaction."

CASE 2.—A primipara, aged 26 years, was in labor about eight hours and was delivered by low forceps and episiotomy and for the first few hours post partum showed no abnormal symptoms. About five hours post partum our attention was called to the fact that the patient was developing a mild shock and this gradually increased until the patient was in a rather severe state of shock. A ruptured uterus was suspected but as the patient did not show any symptoms of shock or hemorrhage immediately following delivery this was partially ruled out. All of the symptoms of shock were present and in addition it was found that there was marked dullness in both flanks so that we made the diagnosis of intra-abdominal hemorrhage of undetermined origin and prepared the patient for operation.

Operation.—The patient was taken to the operating room in profound shock. A blood transfusion was immediately started. Under local novocain 1 per cent and a light gas anesthesia, the abdomen was opened in the midline. The abdominal cavity was filled with a large amount of free blood and clots. The uterus was uniformly contracted and very hard. The ovaries and tubes were normal. After considerable search a bleeding area about 8 by 8 cm. was located low down on the posterior surface of the uterus. There was active bleeding due to a tearing of vessels at this point. An attempt at suturing this bleeding area was without avail so that in order to stop the hemorrhage a supravaginal hysterectomy was performed; the ovaries and tubes were not removed. Following another transfusion the patient was returned to her room in a fairly good condition and left the hospital on the fourteenth postoperative day.

Pathologic Report.—At one point low down on the posterior surface of the uterus was an area about 10 by 10 cm. of deep erosion, there was no evidence of any rupture of the uterus. Sections of this area showed a rather marked decidual formation with hemorrhage on the peritoneal side of the uterus. This formation was in an area of adenomyosis of the uterus, plus an endometriosis.

DR. H. HUDNALL WARE, JR., Richmond, Va.—I would like to emphasize the importance of conservatism in the treatment of endometriosis in young women, and in those women in the childbearing age who want more children.

In 1949 we reported 13 cases of endometriosis and pregnancy. Twelve patients were operated upon because of endometriosis and later had normal pregnancies. In some of these patients one ovary was removed at the time of operation, and in others endometrial cysts were removed from both ovaries, but some normal ovarian tissue was left. In most of the patients adhesions around the Fallopian tubes were freed, and in a few weeks after operation conception occurred.

In one patient the endometriosis was not recognized until the patient was delivered by cesarean section. Twelve patients operated upon because of endometriosis were later delivered of 14 normal term pregnancies. Several of these patients had been sterile for many years prior to the operation for endometriosis.

We have seen young women have two or three normal pregnancies, then develop endometriosis, become sterile, and then, after operation with the removal of some areas of endometriosis and freeing of adhesions, again conceive and deliver normal babies.

Endometriosis is a common cause of sterility in young women. I do not think that the use of contraceptives increases the chances of a patient developing endometriosis, but we do advise married women to have their children early.

Spontaneous arrest of endometriosis does seem to occur in some patients even when pregnancy does not occur.

In conclusion, let me advise conservatism and the preservation of the childbearing function in young women who have endometriosis. Pregnancy frequently occurs in women in the childbearing age after conservative operations for endometriosis.

DR. GAINEY (Closing).—Our observations of other statistically recorded phases of endometriosis are comparable to those in the literature regarding infertility and the incidence of conception following conservative surgery. It was believed for the purpose of this paper, that it was best to report lesions unaltered by surgery or radiation. It was interesting to note that, in clinically recognized cases of endometriosis, there were few with marked growth, those undoubtedly due to decidual hyperplasia and, as mentioned, with spontaneous involution in the last trimester and subsequent regression as noted post partum. This was particularly striking in the case of rectovaginal endometriosis. Comments predicting the reaction, particularly regarding involution of endometriosis, have to be guarded as the clinical observation of the nonpregnant will reveal regression and reactivation of these lesions.

Original Communications

POSTHEMORRHAGIC SHOCK IN THE NEWBORN*

GEORGE Z. WICKSTER, M.D., OAK PARK, ILL.

(From the Division of Obstetrics and Gynecology of Loretto Hospital, and the Department of Obstetrics and Gynecology of Stritch School of Medicine of Loyola University)

THE literature on placenta previa and abruptio placentae, and other causes of occult bleeding from placental or umbilical vessels in the last trimester, impresses one with the lack of emphasis on the role of severe anemia due to blood loss as an important factor in the death of some of the newborn, and the lack of specific directions on exactly what is to be done about such an emergency.

The purpose of this paper is to discuss the various causes of severe post-hemorrhagic anemia in the newborn, and to present cases which exemplify the differential diagnosis and treatment of the condition.

Placenta Previa and Abruptio Placentae

While prematurity and asphyxia play a much more frequent part in the death of infants born in cases of placenta previa and abruptio placentae, their treatment does not demand the immediate decisive action that posthemorrhagic shock does. To quote Wiener:¹ "The hazards to the mother of hemorrhage caused by abruptio placentae and placenta previa are well known, but while it is generally recognized that such cases are attended with high fetal mortality rate due to asphyxia, little or no cognizance is ordinarily taken of the fact that infants born alive in such cases or even in apparently normal deliveries may be suffering from a dangerous anemia due to occult hemorrhage from the placental or umbilical vessels." Macafee² states that the anatomy of the placenta in placenta previa is an important cause of prepartum and intra-partum death of the fetus and postpartum death of the newborn due to exsanguination anemia. A placenta previa is usually a thin placenta which covers a large area of the uterine cavity and is frequently lobulated. Furthermore, the umbilical cord often has a marginal or velamentous insertion which in itself is an added risk. If such a cord is inserted at the lower edge of the placenta in close proximity to the internal os, the first hemorrhage may cause the death of the fetus.

In the past, the emphasis in treatment of placenta previa and abruptio placentae has been focused on lowering the maternal mortality, and with the advent of maternal welfare departments, and maternal death committees, and the easy availability of blood this mortality has reached an almost irreducible minimum. As a result, interest is now being focused on infant survival, as witnessed by the advent of fetal death committees, and much research is being done on the problem of the premature infant. In line with this emphasis on

*Presented at a meeting of the Chicago Gynecological Society, May 18, 1951.

fetal salvage is the importance of looking beyond the immediate expectant treatment of placenta previa, with its marked salvage of the premature infant, and even improved maternal salvage, to the prompt and decisive treatment of certain of the infants born suffering from posthemorrhagic anemia and shock.

The volume of literature on the immediate treatment of infants born suffering from anemia of the newborn or erythroblastosis has focused attention on the necessity and techniques of giving blood to these infants. It has emphasized the necessity of having the equipment ready in every obstetric department for instantaneous use. This has all been for the good. But Wiener¹ has pointed out that infants born suffering from posthemorrhagic shock from the occult placental bleeding of abruptio placentae, placenta previa, and hemorrhage into the maternal circulation, which he has postulated, and in need of immediate massive transfusions, may be considered as having hemolytic anemias of the newborn, and valuable time is wasted getting tests done preparatory to an exchange transfusion when actually a massive regular transfusion should be given, since severe posthemorrhagic anemia, which is often associated with shock, calls for much more vigorous transfusion therapy than does hemolytic anemia. In cases where the mother is Rh positive or, if Rh negative, has neither Rh agglutinins nor glutinins in her serum, the diagnosis of erythroblastosis can be excluded, as a rule, raising in its place the question of possible posthemorrhagic anemia.

Vasa Previa and Other Causes of Bleeding From Umbilical Vessels

Rucker, in reviewing the fifty-two cases of vasa previa in the world literature as of 1944, including three of his own, points out that the important factor in the definition is that a blood vessel unsupported by the cord or placenta should lie over the internal os as it courses through the fetal membranes. Whether the woman is in labor, or the fetus is presenting by the head, or the vessel is near the placenta is not essential to the definition. A velamentous insertion of the cord is usually a prerequisite. But it is possible that (1) a blood vessel running to a succenturiate lobe or between the lobes of a bipartite or multipartite placenta or (2) an aberrant blood vessel leaving an eccentric attachment of the cord and coursing for a considerable distance between the membranes before it penetrates the placental tissues might be involved. When such a vessel overlies the internal os, it is a vasa previa.

Vasa previa has serious potential risks to the fetus. One danger is asphyxia from pressure on the blood vessels, as for example by the fetal head or the insertion of a bag. This is illustrated in Case 2 below in which traction on the Willett forceps caused pressure on the vasa previa by the fetal head with marked slowing of the fetal heart tones. A second danger is rupture of a vessel with serious loss of fetal blood. This tearing sometimes takes place at the time of the rupture of the bag of waters and during the delivery, but it may occur with the bag of waters intact, as in Case 1 below, and early in labor. Velamentous insertion of the cord in itself, without the element of vasa previa, also carries the above risks. Whitehouse⁴ reported a stillbirth due to asphyxia in a case of velamentous insertion of the cord of an infant delivered by cesarean section. Kosmak⁵ reported a case in which a velamentous insertion of the cord ruptured near the entry of the vessels into the upper pole of the placenta in the fundus of the uterus.

In considering the broader problem of rupture of the umbilical vessels reference might also be made to Leff's⁶ case in which there was a rupture of a placental blood vessel which had thrombosed on the fetal surface near the cord with posthemorrhagic death of the fetus before delivery. Busby and

Neal⁷ have reported a case of fetal exsanguination due to the mechanical tear of a small vein at the marginal insertion of the cord as a result of the overstretching of a short cord around the fetal neck at the time of the expulsive efforts of delivery.

Also to be dealt with is the permissibility of including in this definition certain cases in which the umbilical vessels of the type previously described traverse the membranes under the site of the cesarean section incision—here conceivably if too much time is spent in delivering the infant after making the uterine incision, he can lose an appreciable amount of blood before the situation is recognized, either by directly cutting such unsupported vessels, or tearing them in pushing the margin of the placenta aside, or tearing into the richly supplied capillaries and trunks of the terminal villi in the edge of a thin succenturiate lobe. Falls⁸ reported a case of anterior insertion of the placenta which was cut in making the cesarean section incision through the region of insertion of the cord, with resultant fetal shock from the hemorrhage. He states that DeLee referred to this type of case as "placenta previa cesarea." Siddall and West⁹ have recently found in a series of such cases in which the placentas were cut into at the time of delivery by cesarean section that six of the eleven babies showed a moderate to marked posthemorrhagic anemia with the occurrence of shock due to blood loss in at least one of them.

Incidence.—The frequency of velamentous insertion of the cord has been variously stated at around 1 per cent. It was present in 0.84 per cent of Lefevre's¹⁰ 15,844 cases. The condition occurs about nine times more frequently in twins than in single pregnancies, and nearly always in triplet pregnancies. Kobak and Cohen¹¹ in 1935 reported a case of vasa previa in a twin pregnancy with a rupture of the vessels by the first fetus resulting in his death from hemorrhage. A similar case was recently reported by Groseclose.¹² It is worthy of note that while the frequency of velamentous insertion of the cord is about 1 per cent, the incidence of vasa previa is very much less, and that some of the 52 cases reported in the literature are reports of the condition of vasa previa being present with no rupture of the vessels, and no asphyxia, or hemorrhagic shock in the infant. On the other hand, many cases with unruptured vessels go unrecognized or unreported.

Etiology.—The etiology of vasa previa is essentially the same as that of velamentous insertion of the cord, and depends in essence on the abnormalities of the placenta, and cord attachment which result in umbilical blood vessels coursing through the membranes exposed and unsupported by placenta or cord. Von Franque's¹³ explanation of a velamentous attachment of the cord is widely accepted. The cord supposedly rises in the beginning from the most vascular portion of the chorion. If this happens to be in the decidua capsularis, and the development of the placenta is subsequently shifted to the decidua basalis as the vascularity of the capsularis diminishes and the basalis increases, a velamentous insertion results.

Diagnosis.—The diagnosis is based on palpating the pulsating vessel or vessels on vaginal examination after pushing aside the pulsating umbilical cord, if it is present. The condition should be thought of when there is vaginal bleeding at the time of the rupture of the membranes, especially if there is a change of the fetal heart tones. But the vessels may rupture before the rupture of the membranes, or the vessels may not rupture at all. The condition is usually mistaken for placenta previa or abruptio placentae. Graff¹⁴ in 1921 reported that only four out of 51 known cases were diagnosed during labor and that the diagnosis is seldom made before delivery.

Treatment.—Vasa previa is a fetal complication. Fifty-eight per cent of the 52 cases reported resulted in death of the infant. Any change in manage-

ment of the case following the diagnosis is directed solely in the interests of the fetus. Schumann¹⁵ writes: "Should the pulsating vessels be palpated within the cervix, prompt delivery by the most available method is the only treatment." Kosmak⁵ suggests the use of a bag to protect the intact umbilical vessels until conditions are present for delivery per vaginam. Section might be considered either before or after rupture of the vessels in an old primipara if the fetus appears in good condition. The difficulty with this advice is that the condition is seldom recognized until after the rupture of the velamentous vessels, and seldom before delivery. Essentially—the treatment of vasa previa if it is recognized before delivery is much the same as the treatment of prolapsed cord. It is interesting to note that very little is written about the definitive treatment of the infants born with severe anemia due to blood loss resulting from this condition. The treatment of such posthemorrhagic anemia will be discussed in the case reports.

Unapparent Hemorrhage From the Fetal Surface of the Placenta Into the Maternal Circulation

The third part of this paper deals with an interesting and recent hypothesis of occult placental hemorrhage with resultant shock in the infant which is postulated to occur from a break in the fetal placental circulation into the maternal circulation. This was first recognized, and a case published, by Wiener.¹ His postulation of a defect in the placenta which allows fetal blood to flow into the maternal circulation to the point of hemorrhagic shock in the fetus is a novel one and probably as plausible as the hypothesis of such a break as the cause of sensitization in erythroblastosis. In fact, the case given by Wiener¹ was an example of mild erythroblastotic hemolytic anemia with a superimposed posthemorrhagic anemia, both caused by such a placental leak.

To quote Wiener¹ in the discussion of his case: "The simplest way to account for the findings in this case would be to postulate some defect on the fetal side of the placenta. . . Moreover, a slow ooze of the fetal blood from such a placental defect could also account for the extreme anemia, and shock-like condition of the infant at birth. The main objection to this concept is the difficulty of demonstrating such postulated placental defects in pathologic specimens. However, the reason for this may be that such defects need not be large, and as a rule would probably be demonstrated only *in vivo*, as we succeeded in doing in another case recently seen by us. In this other case, the baby was delivered by cesarean section, and at the operation a herniation was found of the anterior uterine wall (due to a previous cesarean section) consisting of a sac about the size of a walnut, and lined only by peritoneum and filled with blood, which ruptured upon palpation."

To further support Wiener's¹ hypothesis of fetal bleeding into the maternal circulation are the following observations. Kline,¹⁶ in an extensive study of normal and erythroblastotic placentas, has demonstrated microscopically the presence of such leaks in the capillaries, villi, and trunks into the intervillous spaces. Bartelmez, in a discussion of Romney and Reid's¹⁷ corrosion and injection studies of the placental circulation, pointed out the ability of the intervillous spaces to take up the amniotic fluid, as evidenced by the case of the late Dr. E. Cornell's in which he (Bartelmez) cut across the intact utero-placental junction of a five months' pregnancy and opened into the intervillous sinuses containing clear amniotic-like fluid. He felt that the replacement of the amniotic fluid about every three hours took place through the mechanism of transudation through the amnion and chorion into the intervillous spaces. He argued that during labor the amniotic fluid would probably be completely

pumped out of the maternal intervillous spaces with every two or three contractions of the uterus.

Similarly one may postulate that late in labor only a traumatic break in the distal zone of fetal capillaries into the maternal intervillous spaces is necessary to account for considerable fetal blood loss to occur into the mother's circulation. Such blood would be pumped into the marginal sinuses and uterine venules of the mother with each contraction.

The fact that many more infants are not born with the anemia of blood loss probably can be explained by the fact that the usual microscopic leaks as described by Kline¹⁶ are not the mechanism in these cases, and that the slow ooze as postulated by Wiener is probably not the pathology here. It may be that the posthemorrhagic shock in the fetus is due to a sudden traumatic unusual break in the fetal capillaries, villi, and trunks during labor with considerable blood loss into the maternal circulation.

Another hypothesis which would also explain such blood loss might also be advanced. One might conjecture that toward the end of labor a traumatic leak in the villi and the distal zone of the short capillaries and the vascular trunks would allow extravasation of blood into the decidual plate of the uteroplacental junction. Enough blood, for example, 80 c.c., could be stored here to cause shock in the fetus and remain until the placenta is separated after delivery. The blood so stored would be easily mistaken as part of the normal third-stage bleeding, as the placenta separated, yet it would be sufficient to cause posthemorrhagic shock in the newborn.

Report of Cases

During the course of this study, four cases were encountered which typify the problems presented in the above discussion of placenta previa and vasa previa. They will be presented in chronological order.

CASE 1.—M. McG., a 27-year-old gravida ii, para i, type O, Rh-positive mother was admitted at term to Loretto Hospital on Nov. 1, 1948, having uterine contractions. The first stage of labor lasted six hours. Just before delivery, the vaginal examination revealed the cervix to be 7 cm. dilated, the head well engaged, and the bag of waters bulging. This was ruptured with a resultant rush of amniotic fluid which was distinctly red in color. A few minutes later the infant delivered spontaneously. The infant was a full-term female weighing seven pounds who appeared very pale and very listless. Respirations were rapid and shallow, and the infant cried weakly. The limbs had little tone, and the liver and spleen were not palpable. The placenta was bipartite, with the vessels to each lobe of the placenta running unsupported through the membranes for the last 16 cm. from the umbilical cord. Several of these vessels traversed the membranes in the immediate region of the artificial rupture of the membranes, but a tear in these vessels was not apparent. Because of the reddish amniotic fluid and the character of the placenta, a diagnosis of posthemorrhagic shock in the infant was entertained. While preparations were being made to give blood to the infant, she suddenly died. The autopsy of the infant was not remarkable except for severe anemia of all the organs.

This case emphasizes the need for immediate differential diagnosis of asphyxia pallida from hemorrhagic shock, and the ruling out of erythroblastotic, hemolytic anemia. The latter is usually quickly done if the mother is Rh positive unless there is an O-A or other rare sensitization. The hypoxia of the anemia of hemorrhagic shock is different from anoxic anoxia of asphyxia pallida in that the infant suffering from the former breathes feebly and rapidly, may even cry weakly, may have a rapid heartbeat, and may make slight body movements and have slight tone, depending on the severity of the shock, while the latter is characterized not only by the paleness which is common to both, but by the ab-

sence of breathing and body tone, and slow heartbeat. The exsanguinated baby does not respond to oxygen by a return of color, while the asphyxiated infant does after respirations are established.

The treatment of the infant suffering from the posthemorrhagic shock of a ruptured vasa previa as presented above is simple, massive blood transfusions. The hypoxia of anemia should be combated with oxygen, while 70 c.c. of blood are drawn from the mother if she is positive or from the department's Type O, Rh-negative blood supply with the Witebsky substance, for immediate direct transfusion of the infant through the umbilical, medial malleolar, or temporal vein. If there is strong reason to believe that the infant presents a posthemorrhagic shock picture, a transfusion of 10 c.c. of blood per pound of body weight of the infant will not harm the baby while a final evaluation is being made. Where the posthemorrhagic anemia is short of severe shock, the proper type and cross-matched blood can probably be awaited. Busby and Neal⁷ recommend the umbilical vein as the best route to institute therapy, using a No. 17 gauge Diamond polyethylene catheter which is inserted for 3 to 3½ inches. Blood is drawn in 10 c.c. aliquots from a bottle of type O Rh-negative female blood by an enclosed system and injected into the infant.

CASE 2.—In the following report of a partial placenta previa with resultant posthemorrhagic shock in the infant it is probable that the tearing of the lip of placenta, which was a succenturiate lobe, was particularly significant because of the large blood supply both from the velamentous insertion which was also a vasa previa, and from the main placental mass directly into the edge of this lobe.

M. G., a 36-year-old gravida ii, para i, at term, was admitted to Loretto Hospital on Aug. 14, 1949, in early labor. About three hours later a considerable amount of bright red bleeding was noted. A sterile vaginal examination revealed an effaced cervix which readily admitted a finger. The circumference of the placenta could be easily palpated overlying the margin of the internal os, and on the anterior left lateral surface of the uterus. This examination caused slightly increased bleeding to occur. Membranes were ruptured, and, following the flow of the amniotic fluid, a trickle of bright red blood was noted. Willett forceps were applied to the scalp, and traction applied to the handle. Fetal heart tones became slow and irregular. The traction was released, the patient was placed in reverse Fowler's position, given oxygen and hypertonic glucose. The fetal heart tones returned to normal. She was taken to surgery where a laparotrachelotomy was done. The infant was a male weighing 9 pounds and 3 ounces, and was markedly anemic. He appeared white and exsanguinated. He breathed very weakly and was flaccid. Liver and spleen were not palpable. The respirations were continued with a tracheal catheter, and 90 c.c. of the pint of blood prepared for the mother were started within 15 minutes in the leg vein of the infant, who responded dramatically in color, tone, respiration, and cry. Two hours later, he again looked very pale, and weak, and another 70 c.c. were given. The infant again responded in a marked manner. Twelve hours later, the baby again began to do poorly and 150 c.c. of blood were given. The infant died 20 hours after birth.

Autopsy revealed a very large defect in the interventricular septum of the heart, one of the largest the pathologist had seen. He felt the death was immediately attributable to this condition. The placenta was described by the pathologist as essentially one with a velamentous insertion of the cord, and succenturiate lobes.

Here the fetal exsanguination took place through the thin edge of the placenta previa which was a succenturiate lobe since it was slightly separate from the remaining body. More important, it was fed by large-caliber umbilical vessels arising from the velamentous insertion of the cord which began 3 cm. away. This thin piece of placenta previa lying next to the os of the cervix was separated from the uterus during labor and during the examination. Holmes¹⁸ states: "The placental separation of placenta previa, and tearing, jeopardize the infant by producing intrauterine asphyxia and fetal anemia." He also writes concerning the causes of death of infants in placenta previa: "Hemorrhage (the third cause of fetal death in placenta previa) may result from placental tearing." Maca-

fee² also emphasizes the importance of the architecture of the placenta previa as causing fetal hemorrhage, especially when large blood vessels feed the margin of the placenta near the cervix as in the case of vasa previa, battledore insertion of the cord, a lobulated placenta, or a succenturiate lobe.

CASE 3.—R. M., a 38-year-old, gravida ii, para 0, whose estimated date of delivery was Sept. 17, 1949, was admitted to Loretto Hospital, Aug. 8, 1949, because of vaginal bleeding which began just prior to entrance. Shortly after admission the bleeding stopped. X-rays were taken and revealed the infant in a transverse presentation. The location of the placenta was not definite in the lateral films, but it seemed to be situated low in the uterus and even bordering the internal os. The patient was placed on absolute bed rest. It was felt that since this was a 34 weeks' gestation, carrying the patient along on expectant management would give the infant a better chance to survive. Because of a hemoglobin of 9.9 Gm. and a red blood count of 3,260 million, she was given a blood transfusion. On Aug. 20, 1949, following another episode of bleeding, a low cervical cesarean section was done. The infant, born in a left anterior scapula position, weighed 4 pounds, 10 ounces, breathed and cried immediately, but his color was ashen. Examination of the chest revealed pulmonary atelectasis. The red blood count was 4.0 million, and the hemoglobin 14.8 Gm. The infant died within 48 hours of birth.

At the time of section, the placenta was found attached to the anterior surface of the uterus, and down over the cervical os. It covered the lower one-third of the incision and exhibited a succenturiate lobe of moderate size with many medium-calibered blood vessels running into it. From a study of the placenta and membranes after delivery, it appeared that the succenturiate lobe was in the region of the trachelotomy incision. It is quite possible that the operator, in separating the upper fourth of the placenta from the uterus in order to get his hand in to grasp the feet of the fetus in the transverse lie in order to do a version and extraction, might well have taken enough time in doing the delivery to allow fetal blood loss to occur from the well-vascularized thin succenturiate lobe and margin of the placenta.

This situation might well be referred to as a case of "placenta previa cesarea" of DeLee, as previously mentioned.

Despite the fact that the autopsy revealed prematurity, atelectasis, and petechial hemorrhages of the brain as the main causes of death of the infant, it seems justified to offer this case as one which also may exhibit blood loss factors. There is a possibility here that anemia was an important contributing factor in the infant's death. Wiener¹ in a discussion of a case of occult placental bleeding from placenta previa feels that the hemoglobin, cell volume, and red blood count do not always mirror the true blood picture, and that while these tests may appear normal as indicated in the above blood count, they may really represent hemoconcentration, while actually there is insufficient blood volume circulating in the vascular system. Taylor¹⁰ and his group have emphasized the inability of the premature respiratory system to reach quickly a proper oxygen equilibrium in the external environment. This situation makes it mandatory not to handicap the infant further by added hypoxia due to insufficient blood volume because of blood loss.

CASE 4.*—M. R., a 35-year-old, gravida iii, para ii, with a 37 weeks' pregnancy, was admitted to St. Anne's Hospital on Dec. 10, 1950, with a painless vaginal bleeding. A diagnosis of placenta previa was made and since the bleeding had practically ceased on entrance, she was treated expectantly because of a history of two previous small infants at term. On December 18, it was believed that the fetus was mature enough to have a good chance to survive and an intracervical sterile vaginal examination was done. It revealed a partial placenta previa.

Increased bleeding resulted. Following artificial rupture of the bag of waters the patient continued to bleed, and a laparotrachelotomy was done. The infant weighed 2,900 grams. Asphyxia pallida was diagnosed and the infant was treated with heat and oxygen.

*This case was given us through the courtesy of Drs. Hawkins, Tierney, and Bartucci.

When the pediatrician arrived he made a diagnosis of posthemorrhagic shock in the newborn based on his one previous experience with such a case associated with placenta previa. While preparations were being made for transfusion, the infant died three hours and ten minutes after delivery. Autopsy revealed severe anemia of all the organs, corroborating the diagnosis of posthemorrhagic shock. The placenta was not remarkable. The obstetrician feels that his digital intracervical examination of the placenta previa caused a tear into the fetal capillaries of the villi and the vascular trunks as the edge of the placenta further separated from the lower uterine segment. Here a diagnosis of asphyxia pallida was first made, when actually posthemorrhagic shock was present. Failure to recognize the condition early enough, and to institute proper treatment, resulted in the death of the infant from acute blood loss.

CASE 5.*—This is a report of an abruptio placentae in which asphyxia pallida was the first and obvious diagnosis, and obscured for a time an underlying posthemorrhagic anemia.

C. W., a 28-year-old, para ii, gravida v, with 37 weeks' pregnancy, entered Cook County Hospital on Feb. 1, 1948, in labor. She had a right lower lobe bronchopneumonia with a temperature of 102.6° F., pulse 140, and respiration 30-35. She was given penicillin. Just before delivery, about 150 c.c. of bright red blood appeared at the introitus. Five minutes later the second stage terminated explosively with the complete expulsion of the fetus, placenta, and membranes, and a gush of blood. Examination of the placenta revealed many adherent clots along the margin. The infant, a 7½ pound male, was born flaccid, pale, and with no respirations. An intratracheal catheter was inserted, supplemented with oxygen. One-half hour later, the infant began to breathe spontaneously, and one hour after delivery was breathing approximately at six times per minute, and was put in a Hess bed with a carbon dioxide-oxygen mixture. The color of the face and head was pale, but the rest of the skin was cyanotic. The lungs were dull throughout to percussion, and moist gurgling sounds were heard on inspiration with marked sternal retraction. It was impossible to elicit a Moro reflex or cry. A blood count on the infant was done and revealed a count of 3.43 million red blood cells. It was thought that the infant suffered from asphyxia neonatorum, atelectasis, and anemia. Seventy-five c.c. of the mother's blood were given through the umbilical vein, and the transfusion was finished two hours, fifteen minutes after delivery. After the transfusion, the repeat red blood count was 3.16 million. Seven hours after birth, the infant died.

In this case, it is probable that the anemia as well as the asphyxia caused the death after the original successful resuscitation of the infant. A more vigorous transfusion therapy might have resulted in a more favorable outcome, although this is doubtful since several factors leading to shock were probably present.

Holmes¹⁸ writes of abruptio placentae: "It is plausible to believe that this act of dehiscence may disrupt the delicate walls of the cotyledon vessels, so that hemorrhage depletes its circulation and anemia is an auxiliary. . . . The ruptured capillaries found in the placenta of some toxic cases would give credibility that death is partly due to hemorrhage." He feels that separation of somewhat less than one-fourth of the placenta, with its accompanying oxygen lack, impairment of nutrition and excretion, plus the possible anemia, toxemia, and prematurity, is enough to prove fatal to the infant.

CASE 6.—This illustrates Wiener's new hypothesis of severe newborn, posthemorrhagic anemia resulting from a break in the fetal placental circulation into the maternal circulation. R. C., a 34-year-old, gravid ii, para i, at term was admitted to Loretto Hospital, on Dec. 29, 1948, in active labor. She was Rh negative, and her husband Rh positive and heterozygous. The first child was Rh negative. There were no previous blood transfusions. Diamond tests taken during her first pregnancy and present pregnancy revealed no antibodies. Her last Diamond test of Nov. 24, 1948, was negative. The nurse's notes twenty minutes before delivery read: "Fetal heart tones fade out, 80-148, quality poor." She delivered a 6 pound, 6 ounce male infant after a labor of three and one-half hours. The baby was very pale and

*This case was given us through the courtesy of Drs. Webster, Mercer, and Christian.

listless. He breathed weakly and rapidly, and did not cry. The liver and spleen were not palpable. Two pediatricians who saw the infant felt that he was in a very poor condition and probably would not survive with any type of treatment. Because the mother was Rh negative, and the infant in anemic shock supposedly from the hemolysis, a diagnosis of severe erythroblastotic anemia was made. It was felt that, despite the fact that the usual findings of enlarged liver and spleen and early jaundice with such a marked anemia of hemolytic origin were not present, the absence of these did not rule out this diagnosis. An exchange transfusion was given the infant, using Rh-negative, type O blood which was available. Specimens of the infant's blood before, during, and after the transfusion were sent to the Samuel Deutsch Serum Center for analysis along with a specimen of the mother's blood. Five hundred c.c. of blood were given to the infant through the medial malleolar vein, and 375 to 400 c.c. of blood simultaneously withdrawn from the umbilical artery. The infant responded dramatically to the treatment and continued to do very nicely during the hospital stay, and has continued to do well to the present. After the transfusion, we learned the results of the tests on the mother and infant. The mother had no saline or blocking antibodies in her blood, and neither did the infant. The infant was Rh positive. The icterus index of the infant's serum was normal. The original count on the infant before transfusion was red blood count 3.68 million, with hemoglobin 13.5 Gm. The differential revealed polymorphonuclear leukocytes 61 per cent, lymphocytes 38 per cent, and polychromasia with 5 nucleated red blood cells per 100 white blood cells counted. All of this supported a diagnosis of hemorrhagic anemia, but there was no obvious basis for such a loss of blood from the fetus except through the placenta and no abnormal condition seemed to involve it: (1) Labor had been normal with no signs of vaginal bleeding; (2) there was no undue rigidity of any part of the abdomen between contractions; (3) the delivery was attended by a normal blood loss before and after the birth of the infant and placenta; (4) the placenta itself had a normal appearance.

Another possibility might be the loss of blood retained in the cord and placenta since we did not (1) give ergotrate with the shoulders, (2) wait for the cord to stop pulsating before clamping it, (3) strip the cord. None of these procedures was done because of the fear of an erythroblastotic infant being born. However, despite the fact that these steps might have given the infant an additional 30 to 90 c.c. of blood, it is not probable that the severe grade of anemia in this case could be accounted for by failure to do them since the infant appeared to be embarrassed before the delivery as indicated by the irregular fetal heart tones.

This case seems to support even more clearly the hypothesis of the possibility of occult placental hemorrhage from a fetal circulation defect than Wiener's case discussed above, since the infant had only posthemorrhagic anemia. One could conjecture that the bleeding from the defect in the fetal circulation directly entered the maternal circulation in quantity enough to cause shock, e.g., 80 c.c., but not over a long enough period to cause sensitization. In fact, such bleeding into the maternal circulation need never cause sensitization in the mother since it is well recognized by hematologists that many Rh-negative women can be given repeated injections of Rh-positive blood without developing antibodies. This was apparently the case here, since the follow-up studies many months later never did reveal antibodies.

Comment

Not infrequently in making the differential diagnosis of posthemorrhagic anemia with shock in the newborn there is no time for the pediatrician to verify the diagnosis, and carry out the emergency treatment. The obstetrician must immediately grasp the situation and institute the blood transfusion, occasionally directly from the mother. He should be as familiar with the immediate treatment of infant hemorrhage emergencies as he is with the hypoxic emergencies. In fact, even if a pediatrician is present, it is the obstetrician who has followed the labor and delivery and has recognized the abruptio placentae or placenta previa with the consequent possible blood loss, as well as the more common asphyxia to the infant. Likewise, in the case of vasa previa and other hemorrhages from the umbilical vessels, it is the obstetrician, who,

on seeing the poor condition of the infant and noting the typical velamentous insertion of the cord with vasa previa, must correlate the pathology and tell the pediatrician what to do. The pediatricians readily admit that, until this condition of posthemorrhagic anemia with or without shock in the infant is more widely written about, and its causes discussed, valuable time may be wasted while they are arriving at a diagnosis, which the obstetrician is in a better position to make. Especially is this true in the Rh-negative mother, in whom the possibility of a severe erythroblastotic hemolytic anemia must be differentiated. Interestingly enough, it was not a pediatrician or an obstetrician, but, as discussed above, a hematologist who sensed the need for and emphasized the definitive treatment of the infant in these cases.

Fletcher's²⁰ and Taylor's¹⁹ recent articles on infant hypoxia are stimulating further interest in the more approved methods of immediate treatment of the hypoxic infant, and this should be paralleled by a growing interest in the possible need for blood in the embarrassed infant—not only in the infant in severe hemorrhagic shock, but the infant in the past who has survived varying degrees of anemia which have gone unrecognized or untreated moderate anemias, which if treated might have hastened a better early adjustment of the infant to his environment.

Every infant born of a case of placenta previa, abruptio placentae, or abnormal placenta should be followed by repeated hemoglobin, cell volume, and red blood counts.

In the very severe cases of posthemorrhagic anemia and shock, 10 c.c. of blood per pound of body weight in the infant should be immediately drawn from the mother, if Rh positive, and given to the infant through the umbilical or medial malleolar or temporal vein. If the mother is Rh negative, plasma should be given to the baby until Rh-negative blood is secured. While this is being done, the infant should be supported with oxygen. Additional blood should be given as the infant's condition demands.

In the slightly less severe cases, type O, Rh-negative blood with the Witebsky substance should be employed. Where there is time, the infant's blood status should be evaluated by the hemoglobin and other blood determinations, and the needed amount of the proper type, and Rh factor blood given.

Conclusions

1. The role of posthemorrhagic shock in the death of the newborn in cases of vasa previa, placenta previa, and abruptio placentae is re-emphasized.

2. Abruptio placentae and placenta previa not only cause fetal and newborn death by asphyxia, interference with nutrition and excretion, toxicity, and prematurity, but also by anemia due to the rupture of the capillaries in the cotyledons in the tearing process.

3. One case of vasa previa, two cases of placenta previa, and one case of abruptio placentae with posthemorrhagic shock in the newborn are cited, and the importance of immediate decisive treatment with massive simple transfusion pointed out. The differential diagnosis from erythroblastotic anemia, and asphyxia pallida, and the differences in treatment are noted.

4. One case of placenta previa, which was also a "placenta previa cesarea," is presented to illustrate potential blood loss factors. The danger of posthemorrhagic anemia whenever even a normal placenta lies under the cesarean section incision is commented on.

5. A case illustrating Wiener's¹ new hypothesis of occult bleeding from a break in the fetal circulation into the maternal circulation as a cause of severe anemia in the newborn due to blood loss is discussed in detail. Certain observations supporting this postulation are advanced. An alternate hypothesis is presented.

6. A plan is suggested for the management of posthemorrhagic shock in the newborn.

References

1. Wiener, A. S.: AM. J. OBST. & GYNEC. 56: 717, 1948.
2. Macafee, C. H. G.: Post Graduate M. J. 25: 297, 1949.
3. Rucker, M. P., and Tureman, G. R.: Virginia M. Monthly 72: 202, 1945.
4. Whitehouse, A. J.: AM. J. OBST. & GYNEC. 33: 527, 1937.
5. Kosmak, G. W.: AM. J. OBST. & GYNEC. 16: 438, 1928.
6. Left, M.: AM. J. OBST. & GYNEC. 22: 117, 1931.
7. Busby, J. G., and Neal, R. F.: AM. J. OBST. & GYNEC. 61: 1173, 1951.
8. Falls, F. H.: Personal communication.
9. Siddall, R. S., and West, R. H.: Paper read before Central Association of Obstetricians and Gynecologists, September, 1951.
10. Lefevre, G.: De L'Insertion velamenteuse de Cordon, Paris Thesis, 1896.
11. Kobak, A. J., and Cohen, M. R.: AM. J. OBST. & GYNEC. 38: 1063, 1936.
12. Groseclose, E. S.: AM. J. OBST. & GYNEC. 61: 80, 1951.
13. Von Franque: Monatschr. f. Geburtsh. u. Gynäk. 12: 128, 1900.
14. Graff, E.: Monatschr. f. Geburtsh. u. Gynäk. 66: 28, 1921.
15. Schumann, E. A.: In Curtis, Arthur H., editor: Obstetrics and Gynecology, Philadelphia, 1933, W. B. Saunders Company, vol. 1, p. 506.
16. Kline, B. S.: AM. J. OBST. & GYNEC. 56: 226, 1948.
17. Romney, S. L., and Reid, D. E.: AM. J. OBST. & GYNEC. 61: 83, 1951.
18. Holmes, R.: In Davis, Obstetrics and Gynecology, Hagerstown, Md., 1950, W. F. Prior Co., Inc., vol. 1, chap. 18, pp. 12, 15, 43, 48.
19. Taylor, E. Stewart, Phalen, James R., and Dyer, Harold L.: J. A. M. A. 141: 904, 1949.
20. Fletcher, J. P., and Rogers, J. W.: J. A. M. A. 145: 553, 1951.

414 SOUTH OAK PARK AVENUE

Discussion

DR. SIDNEY O. LEVINSON.—When Levine and Wiener published their findings on the Rh blood factor and its relation to the pathogenesis of erythroblastosis fetalis, many confusing problems were cleared up. Their work constituted a basis for many new concepts in the field of blood immunology and the need for new standards in blood work. One immediate result was that it became paramount to Rh test all pregnant women and to make sure that when blood was administered it was Rh-compatible blood. By doing this we have overcome hemolytic reactions in obstetrical transfusions which were encountered only too frequently prior to the knowledge of the role of the Rh factor in sensitizing mothers. A corollary to this has been that all individuals requiring blood are being routinely Rh tested, and only Rh-compatible blood is being given to avoid the risk of sensitizing the individual by transfusion of Rh-incompatible blood.

When the profession first became aware of the significance of the Rh factor in the pathogenesis of erythroblastosis fetalis, there was a general tendency to assume that erythroblastosis would occur if the mother was Rh negative and the father Rh positive. Furthermore, if any anemia was encountered in a child, a diagnosis of erythroblastosis was usually made. Such overalertness following a new discovery is not uncommon. The profession soon adjusted its thinking, and a diagnosis of erythroblastosis fetalis was made only when the blood smear of the infant revealed the presence of premature red cells, as well as anemia. As time went on, a greater conservatism was developed in making a diagnosis of erythroblastosis. At the present time, a diagnosis of erythroblastosis fetalis is made only if there is a difference in Rh (or other antigen) characteristic between husband and wife, anemia and characteristic blood findings of erythroblastosis in the infant,

and also evidence of sensitization in the mother's blood and proof of the destructive effect of the sensitizing antigen on the child's red blood cells. The reason for this is that there are other conditions in the newborn that can produce a blood picture simulating erythroblastosis. Examples of such conditions are birth trauma and anoxia. There is need for such critical criteria because of the harm which may be done from a haphazard diagnosis of this condition. Thus, many children are receiving blood transfusions, even when there is no anemia. Furthermore, since the introduction and increasingly widespread use of exchange transfusions, there is no doubt that many infants are subjected needlessly to such exchange transfusions. At present, there is no uniformity on the clinical criteria for employing such an exchange transfusion. Some use it very frequently. One outstanding man in the field uses an exchange transfusion in any infant with definite erythroblastosis whose red blood count is 5 million per cubic centimeter or less. We are more conservative in recommending the use of exchange transfusion and think that greater discretion should be exercised. We believe that in the presence of erythroblastosis with only mild sensitization and red cell destruction of the infant that ordinary transfusions may be adequate. It is our belief that the exchange transfusion should be employed only when the anemia is pronounced, and there is laboratory evidence of a high degree of sensitization and a high titer of sensitizing antibodies in the infant.

As previously stated, anemia of the newborn can occur from causes other than differences in blood antigens. Tonight Dr. Wickster has presented a condition of hemorrhagic shock in the newborn as one of these instances. In considering hemorrhagic shock, I wish to emphasize that our basic principles in the treatment of shock apply. By that I mean that the treatment of shock must be immediate from the viewpoint of restoration of colloidal circulating fluid. If blood is not immediately available, then plasma should be given. Time is of the essence. If the anemia is profound and no Rh-negative blood is available, then Rh-positive blood should be used, although it may well be that plasma will tide the infant over the shock episode until blood can be secured. Clinical judgment, for which there is no substitute, must be applied in the handling of the newborn. There is no set of rules which can be followed blindly. Clinical judgment should be supplemented by the laboratory blood findings of the mother prior to the delivery. If previous tests reveal that there are no sensitizing antibodies in the mother and the newborn child exhibits an anemia, obviously one must look for other causes of the anemia. This is true even in the presence of a difference in blood antigen between husband and wife. Dr. Wickster made one statement that I wish to qualify. He said that if the mother is Rh positive, erythroblastosis need not be considered. This is true in probably 90 per cent of instances. However, erythroblastosis has been encountered in Rh-positive mothers who have Rh-negative husbands due to hr' sensitization. There are a number of other blood antigens which have been discovered, which can also play a role in the production of sensitization and subsequent erythroblastosis fetalis.

In conclusion, I want to stress the importance of adequate laboratory follow-up of blood immunology in pregnant women prior to delivery, the exercise of clinical judgment in establishing a diagnosis in the infant, and, finally, the selection of treatment on the basis of all the facts available.

DR. AUGUSTA WEBSTER.—Dr. Wickster has focused our attention upon hemorrhagic shock of the newborn. He has suggested the very plausible possibility that this condition is more often responsible for stillborn infants and for neonatal deaths than has been generally conceded.

Velamentous insertion of the cord is said to occur in less than 1 per cent of all placentas. Fortunately, in the majority of velamentous insertions the babies are delivered without accident. When infant damage does occur from the rupture of a cord vessel the pathology is apparent and easily recognized by the simple procedure of placental inspection.

Vasa previa is a rare occurrence, and the diagnosis is not often made before birth. In Graff's report only 4 of the 51 known cases were recognized before delivery. This

entity, therefore, although of academic interest, offers very little possibility for remedial therapy.

It seems to me that the main contribution which Dr. Wickster has made in his paper is to focus attention on the possibility of hemorrhagic shock in all pallid infants. Asphyxia neonatorum is always serious, and the consensus is that the prognosis is more grave in the pallid than in the livid infant. These pale, flaccid, feeble babies have a high mortality, both immediate and delayed. Cerebral damage, either from the trauma of labor itself or from the delivery, coupled with prematurity, accounts for a certain percentage of infant fatalities. We have all had the experience, however, of finding nothing more specific upon postmortem examination than severe anemia of all the organs with scattered petechial hemorrhages. Negative findings of this type are not uncommon in a stillbirth associated with placenta previa. Holmes, Irving, and others have long warned of the hazards of infant hemorrhage from torn, low-lying placentas. We, as obstetricians, have continued to accept as inevitable an infant mortality of 15 per cent to 17 per cent in placenta previa while reducing by active therapy the maternal mortality to less than 1 per cent. Certainly, it is high time we turned more of our attention toward these infants, and equipped our birth rooms with transfusion apparatus, and trained obstetric personnel to diagnose and treat promptly infants with hemorrhagic shock.

To borrow a phrase from the Cancer Campaign, if we "think hemorrhage first," and diagnose and treat promptly, we may be well rewarded by an increased infant salvage.

DR. FREDERICK H. FALLS.—Death of the baby in placenta previa is frequently due to cord compression when the insertion of the cord is at the lower margin of the placenta, which is close to the internal os of the uterus. In diagnosing this we make downward pressure on the fundus of the uterus at the same time listening to the heart tones. If they slow up or get very rapid, we feel that the danger of allowing that patient to deliver from below is too great and that she should be delivered by cesarean section.

From the slides that have been shown tonight, I notice that the placentas have all been bipartite. I do not believe that this is incidental, and the same holds for the case cited where the baby lay transversely. In similar cases carefully studied, we have found arcuate or bicornuate uteri. When such a placenta, which is not well developed and not well adapted to take care of the exchange between the mother and baby, is also located on the wall of the lower uterine segment, we often have babies born in poor condition, in anoxemia, and we sometimes have a fetal death.

There is another cause of fatal hemorrhage leading to shock that I think is important to remember in connection particularly with cesarean section. It is a condition that DeLee used to call placenta previa cesarea, that is a placenta on the anterior wall of the uterus and directly in line of the cesarean incision. In order to enter the uterine cavity one must cut through the placenta. As a result it is inevitable that large vessels on the fetal surface or even the cord will be cut. Unless these babies are rapidly delivered or unless the cord is rapidly clamped, they bleed very severely. In fact, I have seen babies die as a result.

I believe the obstetrician is the person who should be responsible for the blood transfusion. I believe that the average obstetrician can transfuse a baby much better than the average pediatrician because he is much more accustomed to carrying out surgical procedures. He should assume this responsibility, and he should familiarize himself with transfusion technique and not waste valuable time waiting for a third party to do the job.

DR. ROBERT GRIER.—There is one point that is very confusing to me. We all have noted fetal heart tones slowing with contractions and when they relax the heart tones pick up. Why do these heart tones slow with contractions? Is it because of compression of the cord as when the cord is around the neck? When there is a compression of the cord and lack of oxygen, the baby's heart tones should become rapid. When the baby is dying as with abruptio placentae the heart tones will first be rapid and then slow and this

usually means the baby is about gone. Why is it when one so frequently listens to the heart tones and finds they are slow that they pick up between pains? I do not know the physiology of this. Can anyone explain?

DR. WICKSTER (Closing).—Dr. Levinson points out that in the differential diagnosis of posthemorrhagic shock, asphyxia pallida, and severe erythroblastotic anemia, the fact that the mother is Rh factor positive does not rule out O-A and other rare sensitizations. In the complete paper for publication this is brought out. But, when an infant is in severe shock, and the mother is Rh positive, it is probably better to go ahead and give the infant an immediate massive simple blood transfusion even from the mother's blood on the assumption that the shock is hemorrhagic in origin, and not a rare sensitization, rather than wait for tests to rule out a very rare condition.

Dr. Fall states that when a placenta previa is associated with a velamentous or battledore insertion of the cord near the obstetric internal os of the cervix, the most common cause of the death of the fetus is asphyxia from compression of the head on the fetal vessels as labor ensues, or compression of a Voorhees bag, or traction on the head by a Willett forceps causing pressure on the fetal blood vessels. However, Macafee emphasizes that hemorrhage from the fetal vessels in the placenta may also cause the death of the fetus because of the proximity of a large blood supply to that part of the placenta which is torn off the lower uterine segment with rupture into the blood vessels in and between the villi. Macafee feels that some of the fetuses die during the first hemorrhage of a placenta previa with battledore or velamentous insertion of the cord near the cervical os, and he cites cases in his series of such fetal deaths.

"Placenta previa cesarea" as is described by Dr. Falls and the late Dr. DeLee could probably be considered under the same nosology as vasa previa as discussed in the paper under the broad definition of vasa previa. There would be value in giving this condition—in which the cesarean section incision jeopardizes the infant by cutting into the velamentous or battledore insertion of the cord or a placenta lying on the anterior surface of the uterus—a label in the textbooks such as the one suggested, in order to further focus attention on the dangers of posthemorrhagic shock to the fetus.

In answer to the question as to the cause of the slowing of the fetal heart tones in asphyxia—in the lower grades of oxygen deprivation of the fetus, the fetal heart becomes more rapid, presumably to hasten the distribution of available oxygen and partially neutralize its diminished concentration in the circulation. However, when the asphyxia is severe as in pressure of the fetal head on a prolapsed cord, or on a battledore or velamentous insertion of the cord, there is stimulation of the vagus nerve in the cardiac center of the medulla with resultant slowing of the fetal heart. After delivery, the slowing of the heart in asphyxia livida and pallida is due to the same mechanism of deoxygenation and hypercarbonation of the vagus center. Undue pressure of the fetal head during labor and delivery also causes stimulation of the vagus by trauma with resultant slowing of the heart, probably again due to oxygen loss and carbon dioxide increase as a consequence of the compression of the medulla with the squeezing out of the blood, causing anemia of the cardiac center of the vagus.

USE OF INTRA-ARTERIAL NITROGEN MUSTARD THERAPY IN THE TREATMENT OF CERVICAL AND VAGINAL CANCER*

J. KEITH CROMER, M.D., JEANNE C. BATEMAN, M.D., G. NEILL BERRY, M.D.,
JOHN M. KENNELLY, M.D., CALVIN T. KLOPP, M.D., AND
LOIS I. PLATT, M.D., WASHINGTON, D. C.

(From the Departments of Surgery, Medicine, and Gynecology of the George Washington University Medical School)

THE local administration of nitrogen mustard (methyl-bis [B-chloroethyl amine] hydrochloride) has resulted in partial regression of malignant tumors which are not amenable to intravenously administered drug.^{1, 2, 3} This therapeutic effect has usually been obtained by repeated injections of the chemotherapeutic agent over a prolonged period of time, through a cannula inserted directly into the artery which supplies the tumor region. This is a study of the immediate effects of HN₂ given by intra-arterial injection in cases of carcinoma of the cervix and vagina.

Material

Sixteen patients from the George Washington University Cancer Clinic and Hospital were treated. Diagnosis was made by biopsy in all cases. Fourteen patients had epidermoid carcinoma, one adenocarcinoma, and one anaplastic carcinoma; fourteen had carcinoma of the cervix, two had carcinoma of the vagina. The age range was from 37 to 71 years, with an average of 53 years. Three patients had received no previous specific therapy for their disease; the others had been treated with hormones, x-ray, radium and/or surgery; singly or combined.

The nitrogen mustard used was methyl-bis (B-chloroethyl) amine hydrochloride.†

Method

The method of delivering the HN₂ to the pelvic viscera by the arterial route has been previously described.² Under general anesthesia a known length of polyethylene tubing was inserted into the deep epigastric or profunda femoral artery and advanced in a retrograde direction through the external iliac artery into the abdominal aorta (Fig. 1). Twenty-three and 28 cm. lengths of tubing, respectively, were introduced. The external end of the tubing was closed with a stopcock which was enclosed in a sterilized plastic bag. For intubating the deep epigastric artery the skin incision was made parallel to and just above the mid-portion of Poupart's ligament. The inguinal canal was opened, the round ligament freed and retracted, and the deep epigastric artery and vein isolated and exposed in the preperitoneal fat along the medial margin of the internal inguinal ring. During the dissection of the artery, one or two small arterial branches were carefully ligated close

*This work was supported in part by a grant from the National Cancer Institute, United States Public Health Service, a grant from the American Cancer Society on the recommendation of the Research Committee, and a grant from the Alexander and Margaret Stewart Trust Fund.

†Supplied through the courtesy of Merck & Company as "Mustargen."

to their origin and divided. Failure to do this interferes with the introduction of the tubing. For intubating the profunda femoral artery, a vertical skin incision was made just below the inguinal ligament and overlying the femoral artery.

After the cannula was in place and before it was permanently anchored, its position was usually checked by an x-ray obtained during the injection through the tube of Diodrast or some other suitable radiopaque medium. Visualization of the tip of the cannula above the bifurcation of the aorta indicated a satisfactory position. Good visualization of the arterial tree was seldom obtained due to the small size of the tubing (0.042 by 0.068 inches). Care must be used in tying the ligatures which anchor the tubing in order to avoid compressing the tubing. The patients were made ambulatory the day following surgery unless they were bedridden for other reasons.

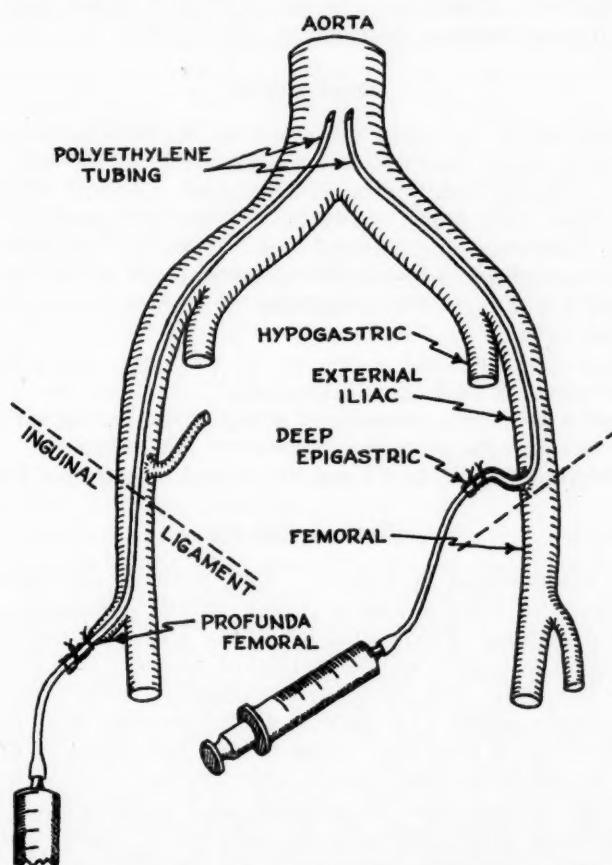


Fig. 1.—Diagram illustrating the method of introducing the polyethylene tube into the abdominal aorta.

HN_2 (2 mg. dissolved in saline) was administered into the tubing every eight hours, preceded and followed immediately by a small amount of saline (1-2 c.c.). The injection was preceded by application of blood pressure cuffs to both thighs and inflation of the cuffs to a level exceeding systolic pressure. The cuffs were deflated and removed three to five minutes following injection. On the few occasions when the patient complained of pain following injection, a 2 per cent solution of procaine hydrochloride was substituted for the saline. An arbitrary total dose of 40 mg. was used in the first few cases but in subse-

quent patients therapy was guided by peripheral blood and bone marrow reaction. Five patients received cortisone (intramuscularly) simultaneously with one injection prior to and one following the course of HN_2 .

Serial cervical smears made by the Ayre spatula technique⁴ were obtained on fourteen patients. Concurrent biopsies on four patients during the course of therapy were also prepared for cytological and cytochemical studies.

On four patients (1, 3, 5, 9) the specimens were of sufficient number to permit complete cytologic studies of the effects of HN_2 upon the cervical cells during the course of therapy. The specimens were stained with Papanicolaou⁵ and Best carmine stains.

Blood counts were made at intervals of 2 to 7 days; and bone marrow studies were done at approximately the same intervals when possible. Hematological studies were done more frequently at the time when maximum depression was anticipated. Therapy was discontinued when the previously described degree of bone marrow depression was noted.⁶

Observations

Table I summarizes the data obtained on sixteen patients. Duration of disease varied from eight years to one month with an average of slightly less than two years. Symptoms included abnormal vaginal bleeding; pain (in abdomen, back, hips, and legs); dysuria, urinary frequency; perirectal pain; melena; fatigue, anorexia, and weight loss. With the exception of the single patient with vulvovaginal epidermoid carcinoma, all of the patients had had irregular vaginal bleeding. Pain was the next most common symptom and was severe in nine cases.

Previous therapy included x-ray in 11 patients, radium in 3, hormone therapy in 5, and surgery in 5 (2 colostomies).

Three patients had two courses of HN_2 . In five patients there was an interruption of several days in the course of HN_2 therapy. The total dose administered ranged from 24 to 82 mg. (0.31 to 1.36 mg. per kilogram of body weight).

Clinical Effects

Results are summarized in Table I. Two patients demonstrated dramatic clinical improvement. Case 4 had a frozen pelvis, colostomy, and uremia of several months' duration. Prefrontal lobotomy had been considered for relief of her pain. Within two days of institution of therapy this patient was eating ravenously and her pain had decreased markedly. Bedridden on admission, she soon became ambulatory. In spite of a continuously high blood nonprotein nitrogen she lived for 2 months. Case 9 had had dysuria and urinary frequency (every 15 minutes, with continuous urgency) prior to therapy. The relief of these symptoms was remarkable and continued for four months. With control of the urinary difficulty the patient was able to sleep in comfort. Some degree of pain relief was observed in the majority of the patients treated.

Side effects of the therapy included some nausea in eight patients (never as severe as that anticipated with intravenous HN_2 therapy), oozing at the cannula site following discontinuance of therapy in two patients, and extravasation of mustard into soft tissue in one patient. Infection at the cannulization site occurred in two patients.

Effects on Lesion

The local effects of intra-arterial injection of HN_2 in the cases studied can best be described by grouping the patients according to the type of lesion present.

Group A.—Four patients (9, 12, 13, 14) presented lateral pelvic wall masses with the local intravaginal disease controlled. All had received heavy irradiation. The incidental radiation fibrosis with partial closure of the vagina in three (9, 12, 13) and a complete colpocleisis in the fourth (14) limited to some extent the objective appraisal of the local HN_2 effects and prevented the securing of photographs or adequate biopsies. Case 13 also had a rectovaginal fistula for which a colostomy had been performed.

Two cases (9, 14) developed necrosis and ulceration of the vagina during and subsequent to the course of the therapy. In Case 9 there was a decrease in induration and a softening of the entire vaginal vault by the seventh day of therapy, ulceration of the apex of the vagina by the second week and complete necrosis of the vaginal vault by the fourth week. Biopsies obtained from the margins of the crater on the fifteenth and seventeenth days of therapy revealed epidermoid carcinoma showing " HN_2 reaction." Minimal softening of the parametrial and lateral extensions accompanied the vaginal changes.

Case 14 developed a complete necrosis of the vaginal mucosa down to the mucocutaneous junction by the ninth day of therapy. The accompanying softening of the left lateral pelvic mass in the patient progressed to the formation of a large necrotic abscess which ruptured into the rectosigmoid on the thirty-third day of therapy. At autopsy, sections of the area involved in the perforation revealed necrosis and gangrene of the entire thickness of the wall. One area from the wall of the tumor mass revealed a small focus of cancer cells. Other sections revealed keratinization and necrosis.

In Cases 12 and 13 no appreciable alterations in the extent and consistency of the involved area in the lateral pelvic wall were noted during the course of therapy.

Group B.—Four patients (2, 4, 5, 10) represented far-advanced recurrent cervical cancer, three following heavy irradiation and one after a radical hysterectomy. All had advanced intravaginal disease. Case 4 had a large rectovesicovaginal fistula and a colostomy. Case 2 was incontinent of urine and feces and paralyzed in both lower extremities.

Local HN_2 effects occurred in two cases (5, 10) and consisted of necrosis of the vaginal mucosa in one (10), and ulceration and necrosis of the cervical lesion in both. There was a concomitant discoloration of the skin of the lower abdomen and loss of pubic hair in one (5), first noted on the eighth day. The changes in the vaginal mucosa (10) progressed from softening to the extrusion of the entire mucosa as a vaginal cast leaving a clean granulating base. By the third day in both, the cervical lesions were softer, more ulcerated, and the vaginal discharge was more copious. By the fourteenth day both cervixes had been converted into large craters with moderately indurated edges. Biopsies from the cervical lesions showed early HN_2 changes on the third day and advanced changes on the fifteenth day of treatment. Moderate changes in the consistency of the pelvic masses were recorded in both cases during the course of therapy.

Two patients (2, 4) failed to show conclusive clinical changes in the local disease or palpable alterations in the size or consistency of the pelvic lesions during the course of therapy. Tissue sections from the margins of the rectovaginal fistula in one (4) revealed early HN_2 changes in the rectal mucosa. The postmortem study of lymph nodes in the other (2) revealed extensive destruction of the nodes within the field of therapy and no changes in the nodes above this area.

Group C.—Seven patients (11, 15, 7, 1, 3, 6, 8) presented clearly visible lesions which permitted maximal objective appraisal of the HN_2 effect on the primary lesion. Three (7, 11, 15) had not received any previous form of

TABLE I. SUMMARY OF CLINICAL DATA ON USE OF FRACTIONATED INTRA-ARTERIAL HN₂ THERAPY IN THE TREATMENT OF CERVICAL AND VAGINAL CANCER

CASE	DIAGNOSIS	ONSET SYMPTOMS	PAST GYN- COLOGICAL HISTORY	PREVIOUS THERAPY	NITROGEN MUSTARD		RESULTS	SIDE EFFECTS	PRESENT STATUS
					TOTAL MG./ KG.	DURA- TION			
1 E. W. N. 37	Epid. Ca. cervix vagina, recurrent	Jan., 1947. Vaginal bleeding, pain in left hip	Blood tumor removed from cer- vix, 1946	X-ray and radium 1947-1948 Rad. hys- terectomy	50 mg. 0.9 36 mg. 0.71	5-2 to 6-2 6-7 to 6-8 11-23 to 11-27 12-7 to 12-9	Reduction in size of lesion. Decrease in surrounding indura- tion; healing cra- ter; relief of pain left heel, nausea	Ulceration and oozing at site of cannula. Pain in left heel, nausea	April 1951, prog- ressive lesion. Repeated vaginal hemorrhage, as- thenia
2 E. M. N. 51	Epid. Ca. cervix Stage IV R. & V. vaginal fistulas	March, 1950. Spot- ting; bowel and bladder inconti- nence, paralysis both lower extremi- ties. April, 1950	Radium in- sertion, 1933, for excessive bleeding	Progesterone Rad. hys- terectomy 1949	40 mg. 1.3	6-19 to 6-25	No change	None	Died 7-6-50. Post- mortem examina- tion revealed marked destruc- tion lymph node
3 A. A. N. 46	Epid. Ca. cervix Stage III	July, 1949. Post- coital bleeding, metrorrhagia; mel- ena, urinary burn- ing and frequency	Regular pe- riods until July, 1949	Stillbestrol. X-ray therapy	40 mg. 0.65	6-8 to 6-14	Healing of crater in left vaginal fornix. Decrease in sur- rounding induration	Aplastic bone mar- row	Subsequent re- peated hemor- rhage. Died 8-6- 50
4 E. R. N. 62	Epid. Ca. cervix Stage IV R. & V. vaginal fistulas	Vaginal bleeding, 1948. Rectal bleed- ing, 1949. Severe pelvic and leg pain	Menopause, 1936	X-ray ther- apy, 1946 Colostomy, 1934	40 mg. 1.1	6-12 to 6-18	Marked decrease in pain and bleeding. Increase in appetite and activity	None	Died in uremia 8- 23-50. At post- mortem, exten- sive ca. hydro- nephrosis and pyelonephrosis
5 M. S. N. 50	Epid. Ca. cervix Stage III	Vaginal bleeding and discharge, 1949; suprapubic distress and cramps	Menopause, 1948	Premarin Radium and x-ray 1950. Exp. lap. and epi- dural block, 1950	50 mg. 0.9	5-26 to 6-8	Slight decrease in size of pelvic mass and softening of indura- tion	None	Died in uremia 8- 22-50
6 G. S. N. 42	Epid. Ca. cervix Stage III	March, 1950. Metror- rhagia; pain left hip, back, pelvis, and abdomen	Periods reg- ular until March, 1950	X-ray	46 mg. 0.77	8-24 to 9-1	Healing of local lesion	Nausea	Subsequent x-ray given
7 F. C. N. 59	Epid. Ca. Cervix Stage III	March, 1950. Vaginal bleeding. Perirectal pain	Menopause, 1941	None	70 mg. 0.7	10-3 to 10-9 10-13 to 10-18	Cervical lesion de- creased by half	None	Subsequent x-ray given, local skin changes, marked

8	Epid. Ca. cervix	October, 1949	Post-regular	na. X-ray	40 mg. 0.8	10-11 to	Reduction in size and	Necrosis and	Subsequent hemor-
---	------------------	---------------	--------------	-----------	------------	----------	-----------------------	--------------	-------------------

8 M.L. N. 48	Epid. Ca. cervix Stage II	October, 1949. Post-coital bleeding, menometrorrhagia, pain, lower abdomen	Regular periods until Oct., 1949	X-ray	40 mg. 60 mg.	0.8 1.27*	10-11 to 10-17 1-18 to 1-28	Reduction in size and partial healing of cervical lesion	Necrosis and oozing at site of cannula.	Subsequent hemorrhage and uremia. Died 4-23-51
9 M.F. N. 49	Adeno. Ca. cervix Stage III Colpocleisis	Bleeding, 1949, pain in back and legs; severe dysuria, urgency and frequency	Menopause, 1949	Progesterone, X-ray, 1949	46 mg. 50 mg.	0.8 0.86	5-26 to 6-1 6-5 to 6-7 8-24 to 9-1	Decrease in pain and bleeding, relief of dysuria; shrinking and softening of lesion	Nausea and vomiting	Slow deterioration, anemia, edema. Died 11-24-50
10 C.S. N. 64	Epid. Ca. cervix Stage III	Jan., 1949. Vaginal bleeding	Menopause, 1935	X-ray, 1949	54 mg.	0.9†	11-2 to 11-10	Grayish necrotic slough leaving vagina clean; decrease in pain	None	Returned to West Virginia
11 A.D. N. 45	Epid. Ca. cervix Stage II	Sept., 1950. Vaginal bleeding	Surgical menopause, 1945	None	66 mg.	1.2	11-10 to 11-21	Cervix reduced in size, crater reduced in depth and cleaner	None	Subsequent x-ray and radium given
12 A.H. N. 67	Epid. Ca. cervix Stage III Colpocleisis	Feb., 1950. Vaginal bleeding; indigestion and fatigue, severe constipation, pain in lower abdomen and back	Menopause	X-ray and radium, 1950	82 mg.	1.36*	12-14 to 12-27	Course unchanged	Mild inflammation at site of cannula	Died 2-14-51. Post-mortem examination showed widespread metastasis
13 M.H. N. 56	Anaplastic Ca. cervix, Stage III Colpocleisis	1946, pain in back and left hip; vaginal and rectal bleeding, 1947.	Hysterectomy, 1944. Fibroids	X-ray, 1947. Colostomy, 1948	24 mg.	0.31*	12-14 to 12-18	Lesion unchanged. Massive inflammatory hip lesion followed by fibrosis of thigh	Extravasation HN ₂ into soft tissues of thigh	Course unchanged
14 M.R. N. 51	Epid. Ca. cervix Stage III Colpocleisis	1946, pain in back and left hip; vaginal bleeding, 1947	Radium for bleeding, 1942	X-ray 1946-1947	58 mg.	0.97*	12-19 to 12-28	Marked softening of lateral (left) pelvic mass with rupture into rectosigmoid moid	Bladder irritation. Nausea and vomiting	Died 1-21-51 after rupture of mass into rectosigmoid and pelvis
15 R.H. N. 48	Epid. Ca. cervix Stage II	1949. Vaginal discharge, pain in right hip and groin	Regular periods	Conization, 1950	40 mg.	0.67*	12-19 to 12-25	Moderate reduction in size and substance of cervical lesion	Refused further HN ₂ . X-ray and radium given	
16 J.S. N. 71	Epid. Ca. vulvo-vaginal	Burning on urination, pain and pressure in perineum	Menopause, 1929	Progesterone, vulvectomy, 1950, excision local recurrence and groin dissection, 1950	54 mg.	0.68*	2-19 to 2-25 3-2 to 3-7	Slight regression	Cardiac arrhythmia. Pulmonary embolism. Nausea	Continuation of HN ₂ . Slow increase in extent of lesion

*Cortisone concurrent.

†Cortisone following HN₂.

therapy except cervical conization in one (15) at the time of the initial biopsy. Four (1, 3, 6, 8) had residual local disease; three after external x-ray therapy for Stage III cervical lesions, and one after external x-ray, interstitial radium, and a radical hysterectomy for a primary epidermoid carcinoma of the vagina. In all seven patients, visible and palpable evidence of regressive alteration in the tumor mass was demonstrable during the course of therapy. This consisted of a distinct reduction in the size of the visible portion of the lesion, as well as a reduction of the palpable extent of the tumor mass.

The earliest changes were more clearly defined in the three previously untreated cases, and appeared about the third day of treatment. They consisted of moderate hyperemia, softening of the entire vaginal mucosa and cervix, and an increase in vaginal exudate. The vascular enrichment produced a bluish discoloration which resembled Jacquemier's sign of early pregnancy and was best seen on speculum examination. Reduction in the size and substance of the cervical lesions was apparent by the fourth day and marked by the eighth day of treatment. In the crater type of lesion (11, 15) the entire cervix became smaller, the ulcer more shallow, and the margins cleaner. The margins of the crater became hyperemic and the base was covered by a necrotic membrane. By the end of the fourth week the entire cervix had been reduced in size and substance by more than 50 per cent and was converted into a plate crater with a small, firm, and hyperemic rim.

In the exophytic type of lesion (7), destructive changes were noted by the sixth day of treatment but were confined to the right half of the lesion which had necrosed and sloughed. Because of this unilateral effect the cannula was reinserted on the opposite side and treatment resumed. By the seventeenth day of therapy the entire cervix had been reduced to one-half its original size.

Two patients (7, 11) developed a reddish discoloration of the skin of the vulva, perineum, and inguinal regions, and one (11) had unilateral loss of pubic hair by the eighth day of treatment.

In the remaining four patients (1, 3, 6, 8) (previously irradiated) local HN_2 effects were similar to those described in the untreated group, except that the changes were more intense and prolonged. The three patients (3, 6, 8) in this group with cervical lesions presented fairly well-healed craters with clean, granulating rims by the twentieth day from the beginning of therapy. One patient (8) revealed areas of local necrosis on the lateral walls of the vagina at the fourth week. Maximum effect was reached at five weeks.

Patient 1, who had vaginal recurrence, showed progressive ulceration with sloughing which continued for a period of three months after the onset of HN_2 therapy. By this time the area of destruction had reached the lateral wall of the pelvis. The crater which remained presented a clean granulating base with little induration around the edges. Tissue sections from the margins of the crater failed to reveal carcinoma at that time. The area of separation corresponded to the area of induration noted prior to therapy. A second course of therapy was followed within two months by hemorrhage and histological proof of recurrence of the disease.

One patient (16) presented a large vulvovaginal recurrence following a radical vulvectomy for a primary epidermoid carcinoma of the vulva. Slight regressive changes were observed in this case following the HN_2 therapy. Subsequent tissue sections following removal of the lesion four months later revealed areas of necrosis attributed to HN_2 .

As mentioned above, five patients received cortisone simultaneously with the nitrogen mustard, one prior to and one following the course of nitrogen mustard. In no instance was there any evidence of enhancement of the local HN_2 effects which could be attributed to the use of the steroid.

Microscopic Changes

Pretreatment biopsies revealed epidermoid carcinoma in every case, and radiation reaction in three cases. Routine histopathological studies on serial biopsies obtained during and subsequent to HN₂ therapy revealed changes identical to those previously described. Changes attributed to HN₂ effects in this series were most clearly depicted in successive biopsies obtained from the previously untreated cases.

The earliest changes were observed on the fourth day and consisted of intracellular edema, swelling and distortion of the tumor cells, and a condensation of nuclear chromatin. By the sixth day there was a definite decrease in the population of the tumor cells and areas showed a tendency to keratinization. Sections on the thirteenth day revealed marked destruction of tumor cells. A large amount of cellular fibrous stroma was an associated finding.

Sections removed from cervixes previously irradiated revealed similar changes and radiation reaction. Apparently changes attributable to both agents are so nearly akin as to be practically indistinguishable.

The biopsies from four patients (1, 3, 5, 8) in the series, all previously irradiated, contained no tumor cells, in two (3, 8) on the sixth day, in one (5) on the eighth day, and in one (1) on the twentieth day of therapy. Cancer was noted in subsequent biopsies in three of the same patients after one hundred fifty-four (1), four (5), and fourteen (8) days, respectively. No subsequent biopsies were obtained in Case 3.

Rectal biopsies from two patients (3, 4) on the third and seventh days of therapy revealed HN₂ changes in the rectal mucosa.

Tissue sections were never free of tumor cells at any time during the course of therapy and up to the beginning of x-ray therapy in the three previously untreated patients (7, 11, 15). X-ray therapy was started on the twenty-seventh day, seventeenth day, and sixteenth day, respectively, from the beginning of HN₂ therapy. No tissue changes in the seven patients (8, 10, 12, 13, 14, 15, 16) who received adjuvant cortisone therapy could be attributed to the cortisone therapy.

Cytological and Cytochemical Changes

On two of these patients (1, 3) having visible lesions residual or recurrent after x-ray therapy, the Papanicolaou smears showed malignant cells (Class V). During the period of mustard administration leukocytes, cellular debris, and acidophilic squamous cells became more numerous and malignant-appearing cells more scant or absent. Some malignant-appearing cells showed the vacuolization and disintegrating characteristics frequently described as radiation effect.⁷

In one case (1) the Best carmine-stained smears showed a very marked increase in red deposit in the squamous cells during mustard administration. In three other cases (3, 5, 9) this increase in glycogen was less marked but definitely noticeable. The smears obtained during HN₂ administration from these and ten other cases (representing patients in each of the three groups) showed numerous cornified squamous cells all of which exhibited some degree of pink staining by the Best carmine stain, a finding not noted in all cornified squamous cells on routine smears.

Pretreatment biopsies showing invasive carcinoma stained with Best carmine showed the pink stain very faintly deposited in the normal epithelium while none was seen in the active cancer cells. The tissue sections prepared from specimens obtained during or immediately following a course of mustard showed some cancer cell destruction and an increase in the depth and cornification of the "normal" epithelium. The cells of the normal epithelium showed bright red depositions in the thickened squamous layer and those of the cancer a slight pinkness. No cytologic difference was noted between the specimens

obtained from patients receiving mustard alone and those who received cortisone also.

Hematological Effects of Therapy

The hematological effects of intra-arterial nitrogen mustard therapy are summarized in Fig. 2. Bone marrow depression manifested by a decrease in cellularity and diminution of young forms preceded severe peripheral granulopenia by several days. Where examination of iliac crest marrow was made, an earlier and more lasting depression was noted than that observed on sternal marrow and was attributed to the localized action of nitrogen mustard. In the five patients who received an arbitrary total dose of 40 mg. the resultant degree of hematopoietic depression appeared to be more related to amount of drug per kilogram of body weight than total dose.

The most marked effect seen was in Case 2 who had severe hypoplasia of both sternal and iliac marrow at the time of death. This patient was extremely cachectic prior to therapy; she received 1.3 mg. of nitrogen mustard per kilogram of body weight.

In six patients there was an early transient leukocytosis. A rapidly developing leukopenia, usually maximum at about two weeks but exhibiting great variability occurred in all patients with the exception of Case 13 who had an initial leukopenia and who received only 0.31 mg. HN_2 per kilogram body weight. White blood counts of less than 1,000 were seen in three patients who had received 1.3, 1.36, and 1.27 mg. HN_2 per kilogram body weight per course. The first patient (2) died on the seventeenth day following therapy with a transverse myelitis resulting from massive tumor involvement of the lumbar vertebrae. The other two (12.8) (second course) had received cortisone concurrently with HN_2 ; both subsequently demonstrated marrow regeneration.

As can be seen by the hemoglobin curves in Fig. 2, anemia resulting from therapy was delayed and usually mild. Many of these patients had intermittent vaginal bleeding, a few had renal impairment, which factors themselves are associated with anemia.

Adjuvant cortisone therapy appeared to exert a mildly protective effect on bone marrow. However, since therapy had to be stopped prior to maximum tolerated hematological depression in a number of these patients the series is too small for evaluation. Cortisone administered to Case 10 following a course of HN_2 resulted in more rapid hematologic regeneration than is ordinarily seen. Case 12 showed only mild depression on combined therapy even though she received 1.36 mg. HN_2 per kilogram of body weight. Withdrawal of both drugs simultaneously, however, was followed by prompt, severe depression of both bone marrow and peripheral white blood count.

Comment

The future place of intra-arterial HN_2 therapy in the treatment of cancer of the female genitals cannot be determined from the data available at the present time. That destructive changes can be produced in pelvic cancer by the use of intra-arterial HN_2 therapy has been amply demonstrated. To predict at this time that its use will replace more standard forms of therapy is a gross misstatement.

Anatomically, the female pelvis is ideally arranged for the application of the method. The placement of the cannula above the bifurcation of the aorta requires no particular surgical skill. The distribution of the blood supply below this point ensures almost complete coverage for the entire pelvis. Few other anatomical regions offer quite this opportunity. Reasonable aseptic care in regard to the stopcock while administering the drug is all that is required

to prevent local complications at the insertion site, and care in washing out the tube after giving the drug will insure patency at all times.

The method is less hazardous for the patient than radical surgical procedures and less discomforting than extensive x-ray therapy.

The best results in this series were obtained in the patients with local disease after x-ray therapy. While short of complete control, the results were

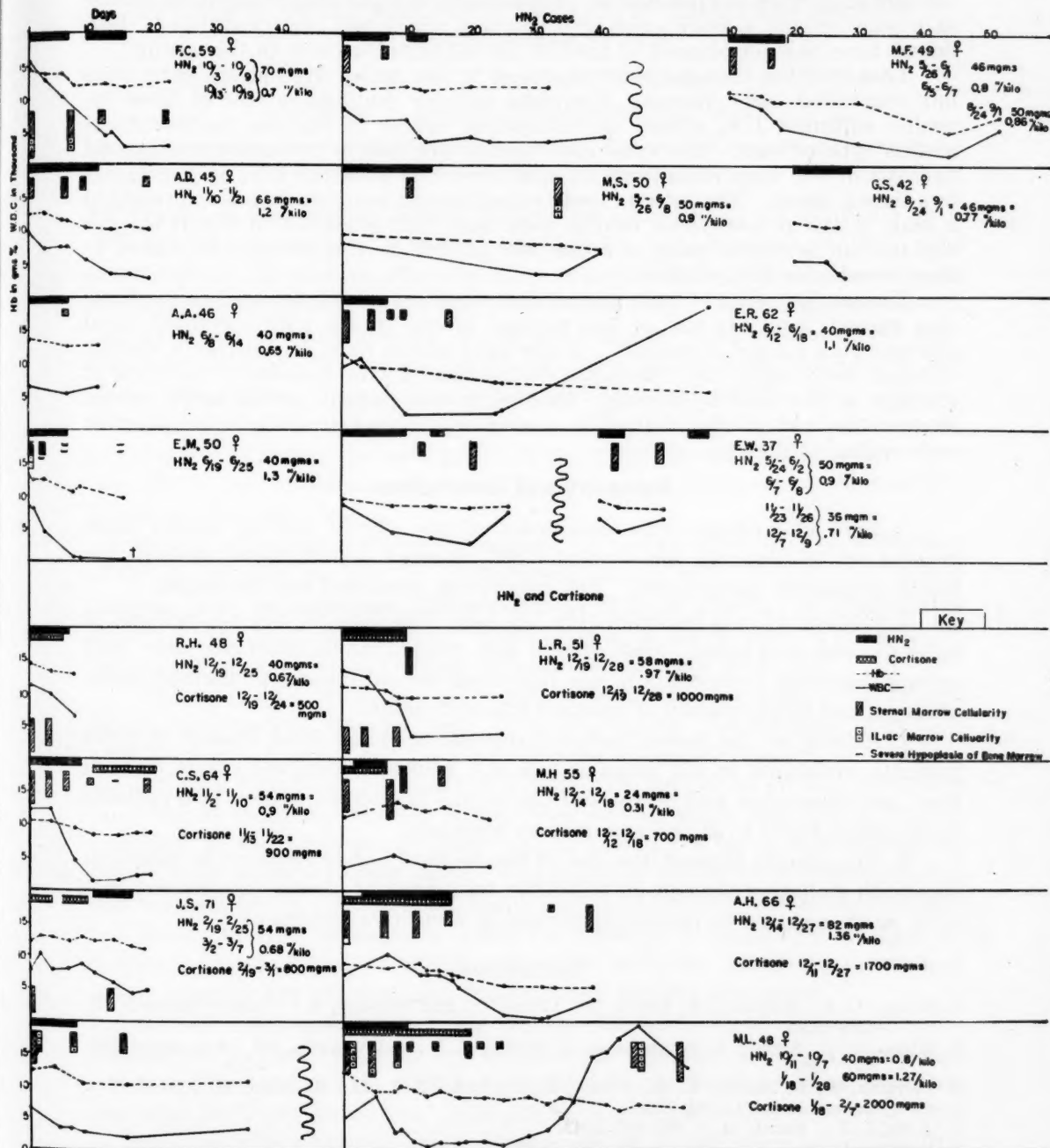


Fig. 2.—Effect of intra-arterial administration of HN₂ on hemoglobin, white blood count, and bone marrow in 16 patients, 3 of whom received 2 courses each. Adjuvant cortisone medication was given either concurrently, prior to or following HN₂ in 7 courses and seemed to exert a mildly protective effect on the hematopoietic system.

more than were expected. The patients were made more comfortable, bleeding and discharge ceased, and the local progress of the disease was temporarily arrested. The incidental vaginal necrosis which followed in two patients was no more severe than additional x-ray would have produced and was to be expected.

The results in the three patients who had had no previous therapy, while encouraging, were not conclusive. Subsequent irradiation produced an intense skin reaction and a heightened local reaction which had been postulated. Sufficient time has not elapsed to predict the ultimate outcome in this group.

Less striking changes were observed in the group with pelvic extensions but controlled local disease. Complete autopsy findings in two of these revealed sufficient HN_2 effects on intrapelvic cancer to warrant further trials in this type of case. The extensive vaginal necrosis in two and rectosigmoid necrosis in one were considered an additive effect from the HN_2 on previously irradiated tissue. The intense local subcutaneous reaction in one represented a leak in the polyethylene tubing with local extravasation of the HN_2 . No explanation is forthcoming for the one patient in this group who failed to show conclusive HN_2 effects.

Except for relief of pain and an improvement in general well-being, little was gained from the use of the method in the group with advanced local diseases plus distant metastasis. While local effects were demonstrable, distant changes were negligible. Regional destruction of lymph nodes at the level of therapy as revealed by autopsy findings in one patient in this series would suggest the use of the method in preventing lateral spreads in conjunction with radiation therapy.

Summary and Conclusions

1. Sixteen patients with carcinoma of the cervix and/or vagina were treated by fractionated intra-arterial HN_2 therapy administered through the lower abdominal aortic route. The results are presented and discussed.

2. Clinical effects included relief of pain and dysuria and an increase of appetite and well-being. Side effects and complications observed were mild nausea, bleeding from cannula site following discontinuance of therapy, hemorrhage, and extravasation of mustard into soft tissue.

3. Effects on the lesion included regression of the local disease in eight patients, reduction in the palpable size and consistency of the pelvic mass in four, and ulceration and necrosis of the vagina in four patients. Two patients in the series failed to show a satisfactory response.

4. The results suggest the use of the method either alone or in combination with radiation therapy in palliative treatment of cervix cancer; and possibly as an adjunct to radiation therapy in definitive treatment.

References

1. Klopp, C. T., Bateman, J., Berry, N., Alford, C., and Winship, T.: *Cancer Research* 10: 229, 1950.
2. Klopp, C. T., Alford, T. C., Bateman, J., Berry, G. N., and Winship, T.: *Ann. Surg.* 132: 811, 1950.
3. Bierman, H. B., Kelly, K. H., Byron, R. L., Dod, K. S., and Shimkin, M. B.: *J. Nat. Cancer Inst.* 11: 891, 1951.
4. Ayre, J. E.: *South, M. J.* 39: 847, 1946.
5. Papanicolaou, G. N.: *Science* 95: 438, 1942.
6. Bateman, J. C., Klopp, C. T., and Cromer, J. K.: *Blood* 6: 26, 1951.
7. Spitz, S.: *Cancer* 1: 383, 1948.

1801 EYE STREET, N.W.

EFFICACY OF Rh HAPTEN THERAPY IN THE PREVENTION OF ERYTHROBLASTOSIS*

ROGER W. MARSTERS, PH.D., RICHARD T. F. SCHMIDT, M.D., AND
MARION E. BLACK, M.D., CLEVELAND, OHIO

(From the Department of Obstetrics and Gynecology, University Hospitals of Cleveland and Western Reserve University School of Medicine)

WHEN an Rh-negative woman has become sensitized to the Rh blood antigen(s) the condition is usually considered to be permanent and with rare exceptions all Rh-positive offspring born subsequently will show some clinical evidences of erythroblastosis. Potter¹ reported that of 86 immunized women, each of whom had had at least one erythroblastotic child, a total of 147 children were subsequently born of whom only three infants were Rh negative and free of the disease. Therefore, in definitely immunized patients with a history of having had at least one child affected with erythroblastosis, the prognosis for future pregnancies is poor, although the possibility of having an Rh-negative infant, free of disease, may be offered to those couples where the husband is heterozygous Rh positive.

Several investigators have attempted to prevent the initial sensitization of the Rh-negative patient by counterimmunization with various more potent antigens, but the mass counterimmunization of large numbers of Rh-negative women during the first pregnancy would seem to be impractical. Furthermore, the procedure is of doubtful value once sensitization has occurred.

Theoretically a promising technique of therapy for the already immunized Rh-negative patient would appear to be Rh hapten. Landsteiner originally used the term "hapten" for modified antigens which were incapable of inducing antibody formation, but could still unite with antibodies already formed to the original antigen. The Rh hapten used in this study has been extracted according to the technique of Carter² from human red blood cells usually obtained from outdated bank blood. The material produced by this technique had been shown by Carter to fix complement when mixed with serum containing Rh antibody.³ Presumably when the material is administered to an immunized pregnant patient the maternal Rh antibody would be neutralized before crossing the placenta and fetal damage thereby prevented.

In any investigation regarding the possible value of an Rh hapten preparation for the prevention of erythroblastosis, it should be remembered that less than 5 per cent of the Rh incompatibilities ever result in actual sensitization with antibody formation.⁴ The Rh typing of the infant concerned must be done accurately because about 29 per cent of the offspring of random Rh-

*The Rh hapten employed in this study was generously supplied by Dr. J. M. Maas, Medical Department, Eli Lilly and Company, Indianapolis, Ind.

negative women are Rh negative also, and will have no symptoms of erythroblastosis regardless of whether antibodies are present in the mother. Furthermore, the remote possibility of the delivery of an apparently normal Rh-positive infant following the birth of several severely affected siblings, as has been pointed out by Chown,⁵ must be considered, particularly in a small series of cases. The therapeutic trial of Rh hapten preparations should therefore be largely, if not entirely, restricted to those Rh-negative patients who have been definitely established as immunized by means of repeated, carefully performed, Rh antibody titrations and who present a history of jaundiced, anemic infants and/or intrauterine fetal death in pregnancies of at least 24 weeks' gestation.

Methods

Each of the ten patients studied was confirmed as being Rh negative by finding the typical Rh negative genotype *cde/cde*, i.e., they were negative to the C(rh'), D (Rh₀) and E (rh'') factors. Each patient had a history of having had at least one erythroblastotic infant and the existence of maternal immunization was corroborated by several Rh antibody titrations. In all of the ten cases reported here, immunization to the Rh factor was through pregnancy and indeed nine of the patients had never been transfused. One patient had been transfused several times, but this occurred after the birth of her second infant, who was deeply icteric.

All Rh antibody titrations were first set up and read with saline suspended Rh-positive red cells; the supernatant was replaced with a 1:1 mixture of AB Serum* and 30 per cent Bovine Albumin† and the agglutination again read. All antibody titrations were performed at the same time each week by the same technician using fresh standard reference cells obtained from the same donor. Details of the titration technique employed have been published elsewhere.⁶

Most of the saline-active antibody titers were of only low order and unless otherwise noted all Rh antibody titration end points reported in this paper are of the serum-albumin-active Rh antibody. This Rh antibody is presumably closely related to Wiener's "blocking" antibody.

The Rh hapten employed was prepared according to Carter's² method with minor modifications³ necessary for large batch processing. All preparations were assayed by the complement fixation method and at various times representative lots were submitted to Carter's laboratory for confirmative assay. We believe the material represents a diligent attempt to produce an Rh hapten preparation commensurate with the best information available at the present time. The material was packaged in ampules containing 100 mg. hapten dissolved in 1 c.c. of either sesame oil or 95 per cent ethyl alcohol. All injections were made intramuscularly into the gluteus maximus and there were no discernible systemic reactions from either preparation. The sesame oil preparation was injected directly and caused only momentary discomfort. The alcohol preparation was diluted with 7 to 9 c.c. of saline just before injection to lessen muscle irritation, but the alcohol-emulsion caused prolonged local tenderness and pain which discouraged the use of this preparation. Several of these patients were patch-tested during the first few weeks of therapy using a hapten preparation prepared in this laboratory according to Carter's technique and no local allergic reactions could be demonstrated.

Six of the patients under study received 100 mg. hapten per week and four of these were raised to 200 mg. each week near term. Three additional

*AB Serum-Hyland.

†Bovine Albumin—30 per cent (Special for Rh testing) Armour.

patients were started on 200 mg. each week and raised to 300 mg. at the fifteenth, twenty-fifth, and thirtieth weeks. A single patient was started on 300 mg. in the seventh week but aborted spontaneously in the fourteenth week. The blood specimens for antibody titration were taken immediately before the weekly hapten injection.

Case Reports

CASE 1.—Mrs. V. E. had a normal Rh-positive boy in 1938 followed by a normal Rh-negative boy in 1941. A second husband was the father of her third child, born in 1946. This Rh-positive erythroblastotic infant survived following multiple transfusions. Her fourth pregnancy terminated in a spontaneous abortion at three months. In the tenth week of her fifth pregnancy the Rh antibody titer end point in serum-albumin medium was 1:32 with only weak agglutination reactions in saline medium. Rh hapten in 100 mg. doses each week was begun and the titer apparently dropped slightly but then maintained itself between 1:8 and 1:16 (Fig. 1). In the thirtieth week the hapten dose was increased to 200 mg. Concurrently there was a slight rise in titer which was probably not significant. In the thirty-fourth week she was delivered by elective section at which time the titer in serum-albumin medium was 1:16. The infant weighed 2,700 Gm., was slightly icteric, and the liver and spleen were both enlarged. The hemoglobin was 9.5 Gm., red cell count 3.6 millions, with 63 nucleated red blood cells per 100 white cells. The icteric index was 40; the cord blood was type A, Rh positive, with a strongly positive antiglobulin test. The infant was immediately given a replacement transfusion and is alive and apparently normal when seen in our clinic at six months of age.

CASE 2.—Mrs. H. F. had a spontaneous abortion occurring at three months in 1941. Her husband is homozygous Rh positive. In her second pregnancy she was delivered at term of an infant who soon developed jaundice and anemia with a red cell count of 1.5 millions. This infant was treated with multiple transfusions and survived. In the third pregnancy labor was induced in the thirty-third week because of polyhydramnios and the infant appeared normal at birth except for prematurity. However, he became icteric on the fourth day and died. This patient was seen in our laboratory in the twenty-fifth week of her fourth pregnancy at which time her anti-Rh titer end points were 1:64 in saline and 1:32 in serum-albumin medium. Two additional titrations to establish the base line showed end points at 1:32 and 1:64 in both saline and serum-albumin. Rh hapten therapy in 100 mg. doses each week was begun in the twenty-sixth week and continued to the thirty-seventh week when the dose was raised to 200 mg. per week. The titers varied only between 1:32 and 1:64 (Fig. 1). Two weeks before term fetal movements ceased. Labor was induced and she delivered a macerated erythroblastotic infant weighing 3,336 grams. The placenta was unusually large and edematous. Because of the autolysis a postmortem examination was not attempted.

CASE 3.—Mrs. J. R. had a normal Rh-positive girl in 1946. Her second pregnancy resulted in a profoundly jaundiced female infant, delivered spontaneously in the eighth month, who died within 24 hours. Her husband was homozygous Rh positive. This patient was first seen in our clinic in the tenth week of her third pregnancy at which time her Rh antibody titer in serum-albumin was 1:512 with only trace activity in saline medium. A repeat determination two weeks later showed an end point of 1:128; at this time weekly doses of 100 mg. of Rh hapten were started. The Rh titer thereafter varied from 1:32 to 1:128 with no significant downward trend (Fig. 1). In the thirty-second week there was some diminution of fetal movement and she began to have contractions and vaginal bleeding. A diagnosis of premature separation of the placenta was made and a cesarean section performed. A severely jaundiced, pale, edematous 2,380 gram infant was delivered. Respirations were sporadic and the fetal heart stopped 26 minutes after delivery. The liver and spleen were both more than three fingerbreadths below the costal margins. The amniotic fluid was deeply icteric; the placenta was enlarged, hydropic, and weighed 1,140 grams. The fetal:placental weight ratio was 2.1:1.

CASE 4.—Mrs. H. R. had a boy in 1936 prematurely delivered in the thirty-second week of gestation. The Rh type of this infant is unknown and although he died several hours after delivery, he probably did not have erythroblastosis. Her second pregnancy resulted in the delivery of a female infant who was reported as being "anemic" soon after birth. This child survived but was not available for Rh typing. Her third infant was an Rh-positive boy who was deeply jaundiced and the diagnosis of erythroblastosis was established. After repeated transfusions the infant recovered and is alive and well. This patient was first seen in our laboratory in the eighth week of her fourth pregnancy when her Rh antibody titer end point in serum-albumin medium was 1:512 with only trace activity in saline medium. Three additional titrations within the next two weeks gave end points of 1:128, 1:128 and 1:256. Rh hapten, in 100 mg. weekly intramuscular doses, was begun in the thirteenth week. The titration end points varied between 1:64 and 1:256 with no significant trend (Fig. 1). At an estimated 28 weeks she went into spontaneous labor and delivered a 21.5 cm. macerated fetus, the size indicating that the baby had probably died four to eight weeks prior to delivery.

CASE 5.—Mrs. E. G., whose husband is homozygous Rh positive, had a normal Rh-positive boy in 1936. Thereafter she had four severely erythroblastotic infants and, of these four, only the second survived after repeated transfusions. Her sixth pregnancy terminated in spontaneous abortion in about the twelfth week; during the sixth pregnancy, the anti-Rh titration end points were 1:8 and 1:16 in serum-albumin with only slight activity in saline medium. She was seen in our clinic in the seventeenth week of her seventh pregnancy when her base line Rh antibody titrations were 1:8 and 1:16 in serum-albumin medium, with only trace activity in saline medium. Weekly injections of 100 mg. hapten were begun and the dose increased to 200 mg. in what was calculated to be the forty-first week of pregnancy. The Rh titer end points thereafter varied between 1:4 and 1:8 in serum-albumin medium and remained fairly constant. In the thirty-seventh week medical induction of labor was attempted at another hospital but was unsuccessful. Labor began spontaneously 45 weeks after her last menstrual period and she delivered a 3,584 gram infant who appeared in good condition. The amniotic fluid was icteric; there was no palpable enlargement of the liver or spleen; the hemoglobin was 15 Gm. and the red cell count 5.1 millions. The smear showed 37 erythroblasts per 100 white cells. The cord blood was type B, Rh positive, with a strongly positive antiglobulin test. The infant was transferred to University Hospitals and a replacement transfusion performed. The infant is alive and well at four months of age.

CASE 6.—Mrs. K. A. had a normal Rh-positive infant in 1943. Her second pregnancy resulted in a full-term, slightly jaundiced, Rh-positive infant who survived without treatment. Her third pregnancy resulted in delivery in the thirty-sixth week of a slightly edematous stillborn female infant. She was seen in our clinic in the tenth week of her fourth pregnancy when her Rh antibody titer end point was 1:16 in serum-albumin medium, with only trace activity in saline medium. Repeat titrations to establish the base line level were 1:4 and 1:8. Rh hapten in 100 mg. doses each week was begun in the thirteenth week using the alcohol-saline hapten, but because of the painful reaction following the injections the preparation of hapten in oil was substituted in the eighteenth week. The weekly injection was increased to 200 mg. in the twenty-fourth week with no change in Rh titer. At about the twenty-seventh week fetal movements ceased, no fetal heart sounds were heard, and when the uterus had failed to enlarge during the next month, the injections of hapten were halted. She went into spontaneous labor in the thirty-fourth week and delivered a macerated stillborn infant.

CASE 7.—Mrs. A. M. had a normal Rh-positive boy in 1942. Her husband was homozygous Rh positive and the next two pregnancies terminated in the delivery of infants stillborn shortly before term. The fourth pregnancy was followed in our clinic and the Rh antibody titer end points varied between 1:16 and 1:32 in serum-albumin medium. This

pregnancy was terminated in the thirty-sixth week by cesarean section. The infant was moderately jaundiced with an icteric index of 35, and anemic with the red cell count 2.7 millions. The cord blood was type B, Rh positive with a strongly positive antiglobulin test. A replacement transfusion was performed and the child is alive and well. This patient returned in her fifth pregnancy at which time the Rh antibody base line titer was repeatedly 1:16 with only trace activity in saline medium. Weekly injections of 200 mg. of Rh hapten were begun in the twenty-first week and raised to 300 mg. in the thirtieth week. There was no depression in the Rh titer and the weekly end points continued at 1:16 until the twenty-ninth week when the titer showed a significant rise with some increased activity in saline medium (Fig. 1). In the thirty-first week fetal heart sounds could no longer be heard and fetal movements ceased. She went into spontaneous labor in the thirty-third week and delivered a macerated 795 gram male infant.

CASE 8.—Mrs. J. G. had a normal infant in 1946, who later died of pneumonia. Her second baby was severely jaundiced but survived following multiple transfusions but was not available for Rh typing. Her third child (by a second husband) had typical erythroblastosis. The infant was Type O, Rh positive, with both the liver and spleen palpable at the level of the umbilicus. The icteric index was 180, hemoglobin 8 Gm., and red cell count 1.7 millions. Although a replacement transfusion was performed, the infant never did well and finally died on the nineteenth day. During her fourth pregnancy she was treated with 300 mg. Rh hapten each week beginning in the twenty-first week. The base line antibody titer end point was 1:64 in serum-albumin medium with negligible saline activity (Fig. 1). There was no apparent change in the antibody concentration after hapten administration was begun, and in the thirtieth week the fetal heart was no longer heard. Three weeks later she spontaneously delivered a grossly normal stillborn macerated male fetus weighing 1,765 grams. An autopsy was performed but furnished little information because of the maceration. The placenta weighed 620 grams, giving a fetal:placental weight ratio of 2.8:1.

CASE 9.—Mrs. R. S. had a normal boy delivered at term in 1944 who is type AB, Rh positive. Her husband is type B, Rh positive, and probably homozygous. Her second pregnancy terminated in the delivery at term in 1947 of a male infant, who became jaundiced within 24 hours and died at the age of seven days. No blood grouping studies and no autopsy were performed; it seems likely that this infant died of erythroblastosis. She was seen in consultation prior to the present pregnancy at which time the Rh antibody titration showed negligible activity in saline medium but a one-plus agglutination at 1:32 in serum-albumin medium. Immediately following the first missed menstrual period, three more control titers to establish the base line were taken in the fifth, sixth, and seventh weeks. These three titers also showed end points of 1:32 in serum-albumin, with only trace activity in saline medium. Rh hapten therapy, in 300 mg. weekly doses, was begun in the seventh week with no significant change in the Rh titer. In the tenth week she noticed slight vaginal bleeding which was treated with progestational therapy and absolute bed rest. Arrangements were made to resume hapten injections the following week, but bleeding continued, and, when the uterus failed to enlarge and repeated pregnancy tests were negative, the uterus was curetted. This abortion was probably unrelated to her Rh problem and the hapten therapy. Three postpartum titers were performed at weekly intervals beginning in the sixth week postpartum and showed a significant titer rise. All three end points were 1:512 in serum-albumin medium with no saline agglutinins demonstrable.

CASE 10.—Mrs. M. G. spontaneously aborted early in her first pregnancy in 1946. At this time she received two whole-blood transfusions from donors subsequently shown to be Rh positive. Her next pregnancy resulted in the delivery of a stillborn, icteric, edematous infant in the eighth month. The pathologic diagnosis was congenital hemolytic disease of the hydropic type. Before she became pregnant again Rh antibody titrations were per-

formed and showed negligible saline agglutinins, but a one-plus clumping at 1:32 in serum-albumin medium. Her husband was type B and probably heterozygous. She became pregnant and beginning in the tenth week, injections of Rh hapten, in 200 mg. doses, were begun. The weekly dose was increased to 300 mg. in the sixteenth week. Four Rh titers to establish the base line before hapten therapy (including one performed before pregnancy occurred) yielded results of 1:64, 1:128, 1:64, and 1:64, all in serum-albumin medium. After hapten injections were begun the titer end points were consistently 1:32 or 1:64 with only two end points at 1:128 (Fig. 1.). She was delivered by elective section in the thirty-seventh week of a clinically normal Rh-negative infant who did well without treatment. The infant was type O and the antiglobulin test negative. The Rh antibody titration end points were remarkably constant throughout the entire pregnancy and the antibody concentration was apparently unaffected by either the pregnancy or the hapten injections. The titer in the second week postpartum was still 1:32 and in the sixth week postpartum 1:64. It is apparent that in spite of hapten therapy, no significant change in the Rh antibody titer had occurred throughout the entire pregnancy.

Results and Comment

The clinical and laboratory study using Rh hapten reported in this paper covered a period of ten months during which time all steps in the technique for Rh antibody titrations were scrupulously held constant. All Rh titrations were carried out at weekly intervals by the same technician employing reference red cells freshly drawn from the same donor just prior to running the tests. Under these conditions the Rh titer end points varied perhaps one or two dilution tubes from week to week, but the general tendency was to maintain the same antibody concentration throughout the entire pregnancy. There were no downward trends confirmed by successive determinations, which might be attributed to significant antibody neutralization by the hapten. On the other hand with a single exception, there were no upward trends. The single significant rise in titration level occurred in Case 7 in the twenty-seventh week and was accompanied by an increase in the saline-active antibody concentration. Only one other patient (Mrs. H. F., Case 2) showed significant saline agglutinins. This particular patient maintained a saline titer of 1:32 or 1:64 from the twenty-fifth week through the thirty-ninth when intrauterine death occurred.

Data have been presented in a previous publication⁶ which indicated that unless the test conditions are carefully regulated the Rh titration method is susceptible to significant error. Even when all technical details of the method have been apparently controlled, there appears to be an inherent variation in the end point reading of approximately plus or minus one dilution tube. This variation has been observed and emphasized by Unger.⁷ When this is allowed for, we have generally found the antibody level in definitely immunized Rh-negative patients to be relatively constant and indeed have very rarely observed the complete disappearance of Rh antibodies from the serum of such patients even several years post partum. The repeated determination of Rh antibodies in these women will usually show antibody titers within a narrow range of dilutions depending on the individual patient.

We believe the sometimes rather dramatic and unexplainable variations in the Rh antibody titer occasionally reported in the literature may possibly be due to variation introduced by laboratory technique. There seems to be no question that an Rh antibody titer level may remain absolutely constant throughout an entire pregnancy (i.e., show no rise) and yet severe fetal damage occur.

Our routine for administering the hapten and drawing the blood for titration provided that the blood specimen be taken immediately prior to the

haptén injection. This necessarily allowed a full week following the haptén injection until the Rh antibody level was again determined. Because the haptén might possibly have caused only a transient depression of the antibody

RH SERUM-ALBUMIN ACTIVE ANTIBODY TITRATIONS ON RH HAPTEN TREATED PATIENTS

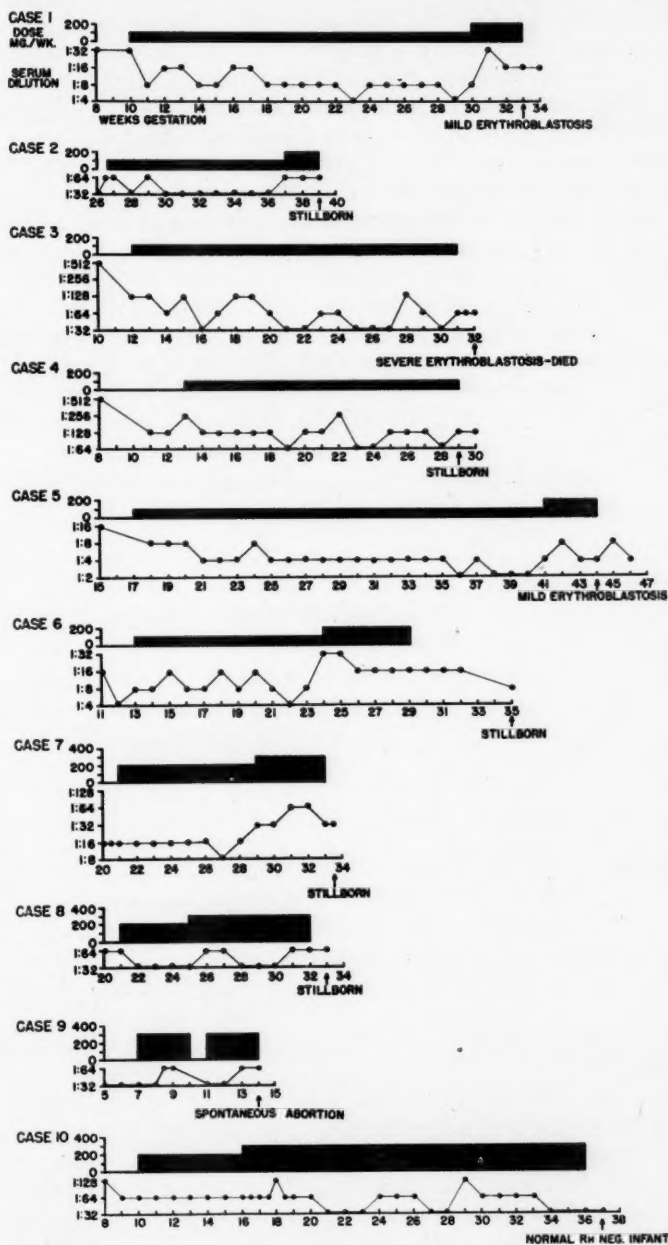


Fig. 1.

level which may have been missed under this schedule three patients had a blood specimen for antibody titration taken 48 hours following the haptén injection. This extra titration was performed on eight occasions and there was no demonstrable fall in antibody concentration in any case.

To check further this possibility, when Mrs. E. G. (Case 5) was two months post partum, four 300 mg. doses of Rh hapten were administered to this patient within a period of one week. Three base line titers determined just prior to this period of injection were 1:8, 1:4, and 1:4. Four additional titers performed during and after this course of relatively high hapten dosage yielded similar results of 1:8, 1:4, 1:4, and 1:8. Therefore, 1,200 mg. of hapten injected into this patient during a single week produced no observable change in Rh antibody concentration. Indeed these postpartum titers on this patient were identical with the titer level which was maintained throughout her pregnancy while receiving hapten. Another patient who had been receiving 300 mg. hapten each week since the fourteenth week of her pregnancy was also given relatively massive dosage in an unsuccessful attempt to halt the rising titer. Three repeat titers before hapten therapy was begun yielded end points of 1:16, 1:32, and 1:32, while four titers performed between the seventeenth and the twentieth weeks showed identical end points of 1:128. She received four 300 mg. injections within a period of one week. However, her titer continued to rise and subsequently four titers at the twenty-second to twenty-fifth week were 1:256 with one result of 1:512. As a result of these discouraging observations, together with our previous results, further hapten injections were halted. Two additional patients who had been receiving 300 mg. weekly injections of hapten for a total of 17 weeks without apparent effect upon the Rh titer were taken off hapten therapy. The weekly antibody titrations were continued temporarily, and there was no significant titer change following cessation of the hapten injections. If the hapten were actually neutralizing Rh antibody then it would seem that the Rh titer level might rise following its withdrawal. This did not occur.

These observations essentially agree with the report of Wolf, Schlutz, Freundlich, and Levinson.⁸ However, the *in vivo* effects observed and interpreted by these investigators as possible evidences of neutralization, i.e., small drops in titer, deceptive prozone phenomena, changes in reactivity of the red cells of infants newly born to hapten-treated women, could not be confirmed. In the 13 hapten-treated patients reported here there was no significant diminution in the Rh titer level in 11 of the 13 patients and, indeed, a rising titer in one patient could not be prevented in spite of large doses of hapten. In the remaining two cases only a very questionable depression of two dilution tubes could be ascribed to possible neutralization effect by the hapten. A total of 267 Rh antibody titrations was performed upon immunized sera in connection with this series of hapten-treated patients and no serologic differences from non-hapten treated patients' sera were observed. The observations reported here also appear to agree closely with those of Spurling, Sacks and Jahn.⁹

The clinical observations are in complete accord with the negative laboratory results and the expected outcome of each pregnancy based upon the individual histories. Of a total of ten cases treated and delivered, the outcome of two may be eliminated from consideration because one pregnancy resulted in an early spontaneous abortion while the other resulted in an entirely normal Rh-negative infant delivered at term. Of the remaining eight cases there were five intrauterine deaths while a sixth infant was so severely affected that he died within a few minutes. Of the two infants who survived, both showed definite clinical symptoms of erythroblastosis. One infant was delivered by elective section at 34 weeks; he was moderately affected but was given an immediate replacement transfusion and progressed satisfactorily thereafter. In this case the early interruption of the pregnancy and immediate replacement transfusion may have been partly responsible for the survival of the infant.

The mother of the other surviving infant had only one child normal at birth, her first born. Subsequent to this four affected infants were delivered, of whom three succumbed, and one survived only after a long hospital course. The next pregnancy terminated in spontaneous abortion. This patient's last pregnancy is reported here, and terminated in the forty-sixth week in the delivery of a moderately affected infant who did well following a replacement transfusion. The Rh titer in this patient hovered between 1:2 and 1:8 and was in the range where clinical damage is usually mild. In view of this patient's long and typical history, however, the survival of this child indicates that the possible value of the hapten therapy cannot be excluded in this particular case.

It is interesting to note that if the Rh antibody levels of these ten cases are arranged according to increasing concentration, the lowest titers are found in Cases 1 and 5. These are the two cases referred to above and resulted in the only infants who survived in our entire series (excluding of course the single Rh-negative infant). This confirms the generally accepted observation that the lower antibody titers usually cause less clinical damage.

Our observations, in regard to the effect of Rh hapten injection upon the circulating antibody titer as well as the clinical results, stand in sharp contrast to the encouraging reports of Carter¹⁰ and Goldsmith.¹¹ A sesame oil solution of the hapten was employed for most of the injections while as far as we know all of the clinical work of these investigators has been with an alcohol-saline emulsion. This difference of vehicle may be significant although with a few exceptions absorption of the oil at the 1 c.c. or 2 c.c. dose level was apparently complete. At the 3 c.c. dose level, however, some difficulty in absorption was experienced.

The time of beginning the hapten injections and the dose employed may be important. Injections in the two cases with surviving infants were begun in the tenth and seventeenth weeks. The mother of the infant who was not stillborn but died within a few minutes had been injected from the twelfth week on. In the remaining five cases, all of which terminated in stillbirths, injections were begun in the thirteenth, thirteenth, twenty-first, twenty-first, and twenty-sixth weeks of their pregnancies. The weekly dose of hapten given to the two patients whose infants survived was initially 100 mg., and subsequently raised to 200 mg. per week. The patient whose baby died shortly after birth received weekly doses of 100 mg. throughout the pregnancy. The five patients who delivered dead fetuses received from 100 to 300 mg. doses per week.

Conclusions

1. The repeated weekly injection of 100 to 300 mg. of an Rh hapten preparation in 13 immunized pregnant Rh-negative patients caused no significant change in the apparent concentration of circulating Rh antibody.

2. In only two out of eight Rh hapten treated and delivered patients could beneficial results possibly be ascribed to the administration of this particular preparation of Rh hapten under the dose regimen employed.

We wish to thank Miss Helen Karlovee for technical assistance.

References

1. Potter, E. L.: *Pediatrics* 2: 369, 1948.
2. Carter, B. B.: *J. Immunol.* 61: 79, 1949.
3. Henry, H. J.: Personal communication.

4. Levine, P.: Postgrad. Med. 5: 451, 1949.
5. Chown, B.: On Certain Variations in Erythroblastosis Fetalis, Blood, Special Issue No. 2, New York City, 1948, Grune and Stratton, Inc., pp. 155.
6. Marsters, R. W.: Am. J. Clin. Path. 19: 1032, 1949.
7. Unger, L. J.: Am. J. OBST. & GYNEC. 58: 1186, 1949.
8. Wolf, A. M., Schlutz, C., Freundlich, M., and Levinson, S. O.: J. A. M. A. 144: 88, 1950.
9. Spurling, C. L., Sacks, M. S., and Jahn, E. F.: Blood 5: 1125, 1950.
10. Carter, B. B.: Pennsylvania M. J. 52: 124, 1948.
11. Goldsmith, J. W.: Wisconsin M. J. 49: 1, 1950.

2065 ADELBERT ROAD

MODERN TRENDS IN OBSTETRICAL ANESTHESIA*

BERT B. HERSHENSON, M.D., BOSTON, MASS.

(From the Boston Lying-in Hospital and Harvard University Medical School)

AMONG the several purposes of good obstetrics is the major aim to bring every gravid woman through her delivery and postpartum period "alive and well and with a living, healthy infant."¹ The ideal of good obstetrical anesthesia is to assist good obstetrics to achieve its objectives.² The modern trend of recognizing the importance of the anesthesiologist as a member of the obstetrical team is in the direction of progress. This is the most important modern trend in the progressive evolution toward achieving the ideal of good obstetrical anesthesia.

The significant trends are perhaps best considered topically, as follows:

1. Pain during labor.
2. Pain-relieving agents.
3. Regional anesthetic procedures.
4. Inhalational anesthetic procedures.

Pain During Labor

There has been a trend in recent years on the part of some lay journals as well as some medical publications to proclaim that pain during labor is an artificial product of culture and civilization. The same groups claim that "primitive peoples" have painless labor. They would have us return to the practice of a primitive form of obstetrics.³ A second limited trend, based on G. D. Read's hypothesis, is the claim that pains of labor are due to fear. Irving has an interesting comment to make on this point. He says, "It is . . . a constant source of wonder that the vast majority of women face labor with such equanimity. If fear is the cause of pain remarkably little is said about it beforehand."¹ Another trend is the ridiculous claim that labor is painful but that the pain is necessary for the mind and soul of the mother. It is not necessary to emphasize to this group of physicians that no factual data exist to support these preposterous notions.

I do not propose to labor over an academic definition of pain. I am going on the assumption that we all understand what is meant by the suffering patient in labor experiencing pain. There is a time during labor when most patients require pharmacologic analgesic and anesthetic agents. We agree with Javert and Hardy⁴ that the intensity of pain during labor is inversely proportional to the duration of the interval between uterine contractions. Furthermore, the intensity of pain increases as labor progresses, reaching maximum pain during the second stage of labor.

There are many factors that can modify the painful experience. Fear, tension, and anxiety intensify pain perception even in the presence of skin infiltration over the areas of referred hyperalgesia. The environment, the presence of psychic and emotional influences, the presence of acute fever and

*Presented at a meeting of the Section on Obstetrics and Gynecology of the New York Academy of Medicine, Tuesday, Nov. 27, 1951.

endocrine imbalance, all bear a direct influence in modifying the painful experience of a particular mother. The relationship of these and other factors to the painful experience of a laboring patient is complex and their quantitative influence is difficult to evaluate scientifically. Nevertheless, the artful physician will exercise every skill to develop confidence in the parturient patient. The modern trend is to reassure this patient that skill and judgment will be exercised by the obstetrical team to provide her with pain relief consistent with safety for both mother and infant.

We realize that there exists no ideal method which will provide complete pain relief during labor for all patients. The modern trend is to evaluate carefully each patient anesthesiologically as well as obstetrically. The obstetrician in cooperation with the anesthesiologist should determine the time and type of obstetrical anesthesia for delivery before selecting the preanesthetic agents. There is a trend away from the use of massive drug therapy during labor.

Pain-Relieving Agents

The agents and techniques selected for preanesthetic medication as well as those anesthetic procedures selected for delivery should be considered as an integrated plan of approach. Misuse of analgesic drugs in obstetrics is more productive of ill-effects upon both mother and baby than properly administered anesthetic agents. The modern trend is to use less of the central nervous system depressant drugs during labor.

The principal purposes underlying the selection of preanesthetic agents for the obstetrical patient may be briefly summarized:

1. The production of psychic sedation for the mother.
2. The degree of pain relief during labor consistent with safety to mother and baby. This will depend upon the individual parturient, the environment, and the experience and judgment of the obstetrical team.
3. The correction of physiological and biochemical abnormalities related to the medical and other complications of the obstetrical patient.
4. The protection of the patient from the potential toxicity of the agents used for obstetrical anesthesia during the delivery.
5. There should be no alteration in the physiological processes of the labor mechanism. The ideal method of delivery is still dependent upon a well-conducted conservative policy during labor.
6. There should be no depression of the fetal or neonatal vital functions. The agents should, therefore, have a short duration of action so as to permit a greater degree of moment-to-moment control, and be correlated with the plan of obstetrical anesthesia.
7. The accomplishment of a rapid, pleasant induction and controllable maintenance of anesthesia for the delivery.
8. A pleasant emergence for the mother devoid of hazards for mother and baby.

The analgesic agents that have been employed in the past are morphine, heroin, Dilaudid, Pantopon, and other similar preparations. Heroin is the best of the opium derivatives for obstetrical purposes but the federal laws ban the manufacture or marketing of this drug. More recently there has been a trend to synthesize analgesic drugs. Some of the members of this group of synthetic analgesics tried in obstetrics are neperidine (Demerol), racemic methadon (Adanon) and its derivatives, Metopon, Dromoran, and others in various stages of experimental development.

These drugs, both naturally found alkaloids, their congeners and the synthetic analgesic agents, in obstetrics, have some undesirable effects in

common. They tend to alter the labor mechanism and tend to depress the fetal vital functions, thus interfering in the establishment of normal neonatal respiration. These effects are produced in the dosage range and frequency of administration required to produce maternal pain relief during labor. The modern trend is to use less of these drugs during labor and to eliminate their administration during the last three, four, or more hours prior to delivery. This group of drugs has distinct value to rest the patient where labor is to be stopped for obstetrical indications. Morphine in one dose not over 10 to 15 mg. is adequate to meet this purpose. The modern trend of combining scopolamine with morphine when the latter drug is indicated has merit here as well. Scopolamine, in a dosage $1/25$ that of morphine, tends to counteract some of the depressant effects of morphine.

The barbiturates have been used for the past twenty-three years in obstetrics. Drugs of this group vary in the time of onset of action, their duration of effect, their mechanism of detoxification and elimination by the body. The fetal and neonatal mechanisms of detoxification and elimination of this group of drugs are more prolonged when compared to those of the adult tissues. The essential effects of the barbituric acid derivatives are in the production of hypnosis, amnesia, and some degree of pain relief. The latter effect is postulated to be "a sort of pharmacologic lobotomy, or reversible depression of the internuncial spread of pain impulses between the thalamus and the cortex."⁵ The barbiturates are employed also as anticonvulsants. A common practice is to employ barbituric acid derivatives as preanesthetic agents to prevent potential toxicity effects from regional anesthetic drugs. There is a growing awareness that this antidotal action of the barbiturates is negligible when the local anesthetic agent is rapidly absorbed. The present trends in the use of the barbiturates in obstetrics are sixfold:

1. To select the barbituric acid derivative for the particular patient and purpose of employment limited to the early phase of labor.
2. To avoid routine repeated large doses of the barbiturates during labor. This group of drugs can definitely cause respiratory and circulatory depression when overdosage is reached.
3. To control the dosage of both the moderate and rapidly acting barbiturates. Some physicians employ slow intravenous administration for this purpose. It is frequently combined with scopolamine to achieve more satisfactory analgesia and amnesia.
4. To facilitate induction of obstetrical anesthesia.
5. To aid maintenance, especially after delivery of the baby.
6. To prevent and treat some of the untoward effects that arise when regional anesthetic agents are employed.

Our most successful methods in trying to achieve safe obstetrical amnesia and analgesia have included the use of scopolamine. It produces amnesia and psychic sedation for the mother without effecting any essential change of fetal or neonatal respiration. It is an excellent preanesthetic agent in the over-all plan of obstetrical anesthesia. Scopolamine reduces the parasympatholytic effects of secretion of mucus and occurrence of laryngospasm. It has the undesirable effect, particularly when combined with barbiturates, during labor of producing muscle overactivity, especially in the patient with elevated reflex irritability. The practice of administering more barbiturates, morphine or morphinelike drugs, paraldehyde, ether-in-oil, and other central nervous system depressant drugs to control this situation proves to be unsatisfactory. A modern trend is to administer apomorphine hydrochloride in subemetic doses to accomplish the same results more effectively and without

additional hazard to the baby. This therapeutic application aids the progress of labor. This is another instance where the obstetrician and anesthesiologist, working together, can reduce the hazards of labor for both mother and baby.

The field of usefulness for obstetrical anesthesia is ever widening. This is correlated with new interests and advances in medicine and its practice. Complications and accidents may occur with disquieting suddenness during labor and delivery. The early recognition and treatment of disturbed physiology in mother and baby are functions of good obstetrics and good anesthesia. Such physiologic disturbances are not limited to drug administration alone but may be preventable even if necessary accompaniments of other causes. An instance is the proper timing of transfusion of compatible blood as the basic solution to the problem of obstetrical hemorrhage. It is a common but serious error to treat the restlessness arising from a confused state in the obstetrical patient as a consequence of hemorrhage or shock by the use of morphine or other narcotic agents. There is a healthy trend to apply fluid therapy more rationally to the obstetrical patient. The correction of the reduction of plasma proteins, the reversal of the albumin-globulin ratio, the retention of sodium and water in the toxemic patient are receiving better attention. The prevention and control of convulsions by the proper use of intramuscular administration of magnesium sulfate and other adjuvants while stabilizing the patient for delivery is a healthy trend. There is an insufficient awareness that the position during delivery may interfere with the vital functions of the obstetrical patient. The breathing capacity of the patient is most interfered with by the Trendelenburg and lithotomy positions.

A recommendation for a future trend is the further development of the postanesthesia recovery room in the obstetrical unit. This is a further means of preventing morbidity and mortality in obstetrics when such a unit is properly staffed and equipped. The obstetrical patient should not be permitted to return to her unattended room or bed until she is conscious, her airway adequate, the vital signs stable, and the uterus is well contracted. Nurseries should be available for the proper care of the problem newborn patient.

A trend that needs recognition and emphasis is the proper selection of preanesthetic agents, prior to the second stage of labor, based on the plan of obstetrical anesthesia for delivery. There are available today a number of regional and inhalational anesthetic procedures for the latter purpose.

Regional Anesthetic Procedures

The agents available to interrupt the conduction of the nerve impulse at the level of the peripheral neurones are several. Those agents that have received clinical application are procaine, Metycaine, and the longer acting agents, Pontocaine and Nupercaine. More recently Intracaine, Lucaine, and Xylocaine have received some attention. Their field of usefulness in obstetrics remains to be explored. There is a limited trend to use hyaluronidase, or Hydase, as a "spreading factor" for local infiltration anesthesia. Its mode of action is to facilitate the spread of injected materials through an enzymatic effect upon connective tissue hyaluronic acid. It appears to have no merit for regional anesthetic procedures other than local infiltration. Another trend is the use of sympathomimetic amines to prolong the duration of sensory anesthesia during regional anesthetic procedures. Ephedrine, Methedrine, Neo-Synephrine and other vasoconstrictors have been recently explored for this purpose. None seem to be superior to epinephrine.

The regional anesthetic procedures more commonly employed for the obstetrical patient are pudendal block with or without local infiltration, local infiltration itself, spinal intrathecal block, including "saddle block," and

spinal extrathecal block, including caudal or posterior sacral block. Other regional anesthetic techniques less commonly employed in obstetrics are paracervical block, parametrial block, lumbar paravertebral sympathetic block for pain relief, and anterior or presacral block. The modern trend is away from the latter group of blocks because they are time consuming, not predictable, often complicated, and there is risk involved. In some instances the complications include the possibilities of hemorrhage, accidental intrathecal massive injection, and trauma. The intravenous route is also used in a regional anesthetic technique.

Local infiltration analgesia alone or combined with pudendal block for vaginal delivery is an increasing obstetrical anesthetic procedure. Its success varies considerably and it is not a universally applicable procedure. It has the distinct advantage of little or no effect on the fetus but often requires a great deal of patience and tolerance on the part of both the obstetrician and the mother. Local anesthesia, or field block, for abdominal hysterotomy should be reserved for the special problem case and be performed by the most skillful operating team. Otherwise the hazards are greatly multiplied should the local anesthesia prove inadequate. There appears to be a trend to employ local anesthesia more frequently for vaginal delivery but less so far abdominal delivery.

The spinal cord in the adult usually terminates intrathecally at a level corresponding to the second lumbar vertebra, or its corresponding space. Occasionally this takes place at a lower level. The level recommended for injection of the anesthetic solution into the thecal sac fluid is the third or fourth lumbar intervertebral space. A block of the nerve roots will be instituted proximal to their points of origin.

To produce satisfactory pain relief during vaginal delivery and labor by the regional approach, the level or height of sensory anesthesia should approximate the tenth thoracic dermatome. To provide for necessary pain relief during abdominal delivery the level of sensory anesthesia should reach the fifth thoracic dermatome and not infrequently higher levels. Levels higher than the tenth thoracic segment usually block motor pathways of innervation to the uterus and birth canal.

It has been demonstrated⁶ recently that neurogenic tone is increased during pregnancy. Consequently the same woman during pregnancy is more likely to show evidence of severe hypotension accompanying paralysis of the same levels of sympathetic innervation. This method of obstetrical anesthesia has other disadvantages. The patient who exhibits collapse of the vital functions of respiration and circulation is not infrequent. The cause is usually due to the height of spinal anesthesia. A more frequent situation occurs in the case with respiratory insufficiency or embarrassment that may result in a catastrophe if untreated. Great caution should be exercised in the administration of spinal anesthesia to the pregnant patient for her exaggerated lordosis tends to cause insidious ascent of the height of anesthesia. The occurrence of nausea, emesis, retching, and derangements of respiration and circulation are quite frequent during intraperitoneal manipulation, probably reflex in origin. All of these disturbances are more evident under spinal anesthesia.

The number of obstetrical patients having neurological sequelae, following spinal anesthesia, seems to be increasing. There is a trend to reduce the incidence of the distressing symptom of postspinal headache by the use of smaller-calibered spinal needles, and adequate hydration, as well as avoidance of multiple dural punctures. The case of paraplegia and interference with sphincteric function following spinal anesthesia in what appears to be an uncomplicated administration still exists. This type of anesthesia increases the

incidence of operative deliveries when there exists interference with the labor mechanism. The continuous spinal technique carries with it a higher incidence of needle breakage, or retention of sheared catheter fragments, when the latter technique is used.

The advantages of spinal anesthesia are its comparative ease of administration, dominance of parasympathetic activity on the gastrointestinal tract, and comparative absence of fetal effects in the absence of maternal hypotension. In the interest of safety for the obstetrical patient, spinal anesthesia should never be selected "because an anesthesia machine is not available or skillful anesthesia is lacking." A future trend should be more serious consideration of the risks involved when this portal of entry is selected for the administration of obstetrical anesthesia. The benefits to be derived for the mother and her baby should outweigh the immediate and delayed complications that may follow.

Extradural anesthesia is a method of regional anesthesia where the agent in solution is injected through a needle, or catheter, into the potential peridural, or epidural, space. The spinal extradural space is identified by the presence of a negative pressure when the needle is inserted at the third or fourth lumbar interspace. The caudal approach is through the sacrococcygeal ligament at the sacral hiatus into the sacral canal. The purpose of these techniques is to block the extrathecal peripheral nerve root segments with the anesthetic solution in the form of a bath. Here again single-shot or continuous adaptations may be employed. In the latter instance either needles or catheters are used for the injection of intermittent relatively smaller doses of the anesthetic agent.

The chief advantage of the extradural approach over the intrathecal technique of producing obstetrical anesthesia is the infrequency of postspinal headache. The disadvantages of the intrathecal approach are also inherent in the extradural technique. Caudal anesthesia was used in obstetrics over forty years ago by Stoekel.¹ Anomalies of the sacrum limit the selection of caudal anesthesia to about 20 per cent of the cases, even in the hands of the proponents of this technique. Deaths have been known to occur as a result, probably, of accidental intravascular or intrathecal injections. There is a growing trend to select this route less frequently for obstetrical anesthesia.

The extent of the successful obstetrical regional anesthetic procedures varies directly with the skill of the anesthesiologist, the dexterity of the obstetrician, the experience and judgment of both, the cooperation of the patient, and the environment of the conduct of the labor. There is a growing realization that the regional anesthetic procedures are not the answer to the obstetrician's dream of a method of achieving safe, painless labor. However, there is a trend to apply regional anesthetic procedures during the latter part of the second stage of labor in selected obstetrical patients. We have reserved this type of obstetrical anesthesia for patients with respiratory complications, those patients having recently ingested a meal and for whom delivery is imminent, patients at term with fetal distress or with fetal immaturity, mothers with a rising titer of Rh antigens where the baby is to have one or more replacement transfusions, patients with severe or uncontrolled diabetes, and for some special obstetrical reasons like the patient with a long, difficult labor in whom a difficult delivery is anticipated.

Clinical reports have appeared from time to time advocating the intravenous route for the administration of nonvolatile drugs to accomplish obstetrical anesthesia. Among this group of drugs the short-acting barbituric acid derivatives, Evipal Sodium, Pentothal Sodium, and more recently Spirothal Sodium and Surital Sodium have been advocated. These agents act as hyp-

notics, sedatives, and analgesics to some degree. They can produce obstetric anesthesia when a state of acute barbiturate toxicity is induced. Incidentally, the maternal and fetal blood barbiturate concentrations are equal within approximately ten minutes of maternal intravenous administration. The mechanism of tissue distribution and detoxification of barbituric acid derivatives in the adult is still to be established. The detoxifying mechanisms of the newborn are even more obscure. This should prove a fruitful field for future investigation. In our experience the incidence of neonatal asphyxia is increased with the administration of the nonvolatile drugs to accomplish obstetrical anesthesia. Other undesirable results produced by this method of anesthesia are respiratory and circulatory depression, and not infrequently laryngospasm of various degrees of severity. The former effects are due to the central action of the barbiturates and the latter effect is due to the peripheral parasympathetic action of this group of drugs. They are contraindicated in mothers with cardiac or respiratory disease. The dangers to the premature infant are obvious.

More recently clinical reports have been appearing on the intravenous use of the muscle relaxants to reinforce the action, or duration of effect, of other anesthetic procedures. The chief members of this group of nonvolatile muscle-relaxing agents currently receiving attention are Intocostin, Mecostin, Myanesin, Syncurine, Flaxedil, and still others in the experimental stage. This group of drugs is not in any sense an anesthetic agent. Respiratory paralysis is readily attained with this group of curarelike drugs. Respiratory paralysis may occur with a suddenness as dramatic as after a readily obtained overdose of intravenous barbiturate. The combination of these drugs administered intravenously to accomplish obstetrical anesthesia is not to be recommended as a modern trend. The muscle relaxants pass through the placenta and into the fetal circulation. Their clinical application in obstetrical anesthesia is at present in the experimental stage. Their future application in obstetrical anesthesia may well be in those instances requiring muscle relaxation where regional anesthetic procedures are inadequate, or where lighter levels of inhalation anesthesia are desirable.

Inhalational Anesthetic Procedures

The skillful use of inhalational agents to achieve obstetrical anesthesia is more satisfactory to meet the needs of the obstetrician, the anesthesiologist, and the desire and welfare of the mother and her baby. Judicious selection of preanesthetic medication is an integral part of good obstetrical inhalation anesthesia. The drugs selected, their dosage, route of administration, proper timing, their duration of action, the recognition and early treatment of undesirable effects are very essential factors in determining the success of obstetrical inhalation anesthesia.⁸ We have been impressed with the facts that parity, prenatal maternal complications, prematurity, presentation and position, infant complications, prolonged and difficult labor, the nature of the obstetrical procedure, the presence of obstruction in the life line of the fetus as well as the misuse of nonvolatile analgesic agents are more significant etiologically in the production of neonatal asphyxia than is the proper administration of obstetrical inhalation anesthesia.

The inhalational agents that receive application to clinical obstetric anesthesia are nitrous oxide, ethylene, cyclopropane, diethyl ether, divinyl ether, trichlorethylene, and chloroform. Improper or careless administration of these agents constitutes a serious hazard. Respiratory obstruction, respiratory depression, diminution in minute-volume pulmonary ventilation, administration of oxygen-deficient atmospheres, or deficient circulatory transport

medium result in hypoxia and hypoxemia. The resulting tissue oxygen deprivation and carbon dioxide accumulation profoundly affect the mother as well as the fetus in his already existing asphyxial state during intrauterine life. Maternal uterine hypoxemia is not conducive to extrauterine neonatal physiologic activity. On the other hand the relatively large neonatal pulmonary ventilatory minute volume favors the rapid elimination of the inhalational anesthetic agents.

Nitrous oxide in the presence of adequately oxygen-enriched atmospheres still is a very useful agent for obstetrical analgesia and selective anesthesia. This agent is nontoxic, nonexplosive, nonirritating, not detoxified by maternal or fetal tissues, and possesses rapidity and reversibility of action. It is, however, a nonpotent anesthetic agent. Nitrous-oxide-oxygen mixtures containing less than 20 per cent of oxygen, used for periods over three minutes, often result in neonatal asphyxia. There is a trend to use nitrous oxide, in the presence of more than 20 per cent oxygen atmospheres, to facilitate induction of a more potent inhalational agent. The thought behind this application is to permit the use of highly oxygen-enriched atmospheres during maintenance of obstetrical anesthesia. Another recommended trend is to employ nitrous oxide-oxygen mixtures for episiotomy and other vaginal plastic repair during the third and fourth stages of labor. The rationale of this technique is the prevention of uterine relaxation, or atony, from depth of anesthesia as a contributing cause. Another trend is to administer nitrous oxide and oxygen mixtures for purposes of pain relief, but not for muscle relaxation, during the repair of the abdominal wall following abdominal hysterotomy in obstetrics. These are artful applications of nitrous oxide that may require other adjuvants in the practice of good obstetrical anesthesia. Nitrous oxide is still a very satisfactory agent when used for purposes of analgesia. It should never be used for purposes of muscle relaxation when hypoxia is the real mechanism involved. Hypoxia is a powerful method of producing muscle relaxation and rapid anesthesia but at the expense of destruction of cell irritability. There is a growing awareness of the importance of preventing hypoxial states during intra- and extrauterine life not only for the sake of the individual and his family but also for the society in which they may live.

Ethylene is also nonirritating, nontoxic, and possesses rapid reversibility of action. It is explosive like all hydrocarbon gases used in anesthesia. It is the only anesthetic gas that is lighter than air. Ethylene has a somewhat greater potency than nitrous oxide. Administered in the absence of hypoxial mixtures there is a limited place for the employment of this gaseous agent. In some areas there is a tendency to the use of this agent in obstetrical anesthesia. This is not a universal trend.

Cyclopropane is the most potent of the available gaseous anesthetic agents. It has all the merits of such an agent, but possesses the demerits of the hydrocarbons. Cyclopropane has no deleterious effects on any of the maternal parenchymatous structures. It does depress uterine irritability and tonicity at the deeper levels of anesthesia. Judiciously employed to supplement nitrous oxide it is a useful obstetrical anesthetic agent. High concentrations of oxygen-enriched atmospheres are permissible and desirable when this agent is used in obstetrics. Experimentally it is demonstrable that fetal respiration remains intact during maternal anesthesia, corresponding to surgical levels, with cyclopropane. There is a limited trend to the use of cyclopropane for purposes of induction of obstetrical anesthesia, employing ether and other pharmacological adjuvants for the accomplishment of muscle relaxation. Further knowledge and experience of the pharmacologic action of this nonirritating rapidly acting gas are yet to be accumulated before cyclo-

propane can be assessed for its proper use as an obstetrical anesthetic agent. One such example is the anesthetic approach to the obstetrical problem case presenting the complication of hemorrhage where regional anesthetic procedures are generally contraindicated.

The gases acetylene and propylene have been explored to produce obstetrical anesthesia. They have been found to act as convulsants at anesthetic levels. Of the rarer gases, xenon has been observed to possess limited anesthetic qualities. There is no indication, at present, that these gases merit further clinical exploration to achieve safe obstetrical anesthesia.

Chloroform has been both condemned and praised for the past century. It is still used widely to produce obstetrical analgesia and anesthesia in some areas. It is relatively nonirritating, nonexplosive, and rapidly acting. It is an unusually potent anesthetic agent. In the presence of oxygen-enriched atmospheres chloroform can provide profound muscle relaxation even in the lighter stages of anesthesia. Overdosage with this agent, as with cyclopropane, is quite readily accomplished. The possible occurrence of damage to some of the parenchymatous structures should not be underestimated. Controversy as to its safety still continues. Haste in the administration of chloroform may result in grief. However, because of the distinct advantages of chloroform the modern trend is not to discard this agent in obstetrics. It is not recommended for universal application in the practice of obstetrical anesthesia. There is a real need in obstetrical anesthesia for a gaseous agent that will combine the potency of chloroform with the many advantages that nitrous oxide possesses. This is a promising field for future exploration.

Trilene, or purified trichlorethylene, is an unsaturated halogenated hydrocarbon volatile liquid. Overdosage is easily reached when this agent is administered by the closed system. The appearance of dichloroacetylene, as a by-product, is not infrequent by this technique. Whether due to overdosage or the appearance of dichloroacetylene, cardiac irregularities, as well as other preventable complications, have been known to occur during its anesthetic application in obstetrics. Trilene has been used successfully as a supplementary analgesic agent to reinforce the potency of nitrous oxide analgesia. Used in this manner and in the presence of oxygen-enriched atmospheres it appears to have some usefulness in obstetrical anesthesia.

Vinethene, divinyl oxide or divinyl ether, is a liquid volatile anesthetic agent. It possesses about five times the potency of diethyl ether. It is a more satisfactory and safer inducing agent than ethyl chloride. Vinethene serves a useful purpose in obstetrics to potentiate nitrous oxide as a volatile relaxing agent for short anesthetic procedures. The chief disadvantages of divinyl ether are its tendency to produce excessive mucus secretion, fibrillary muscular twitchings, and liver damage when used for protracted periods. The trend is to limit the application of Vinethene to the special purposes previously indicated for obstetrical anesthesia. A few interesting facts and comments on this agent are pertinent. Divinyl ether was synthesized in this country on the basis of combining the merits of ethylene and diethyl ether. It is an example of bringing a combination of pharmacological action and chemical synthesis to bear on the problem of clinical therapeutics. This is another instance of the potentialities of American ingenuity when there is a pooling of the knowledge of the chemist, pharmacologist, and clinician.

Diethyl ether, commonly known as ether, has two disadvantages in obstetrics; one is its irritating salivary effect, often resulting in the production of excessive secretions in the lighter planes of anesthesia. The other is its slowness of action, resulting in delay of induction into and emergence from anesthesia. Exposure to sudden high concentrations of ether vapor may

result in varying degrees of laryngospasm. Reflex closure of the vocal cords should not be confused with other preventable causes of respiratory obstruction. A resourceful anesthetist can usually circumvent these disadvantages of ether.

Diethyl ether has many advantages in obstetrics. It is a potent drug permitting respiratory administration with highly oxygenated atmospheres. Ether possesses the widest margin of safety of all available anesthetic agents. It is retrievable without added load on the body's detoxifying mechanisms and without essential residual damage to the parenchymatous structures. Ether has the desirable sympathomimetic actions of increasing cardiac output, and coronary blood flow, and relaxing bronchiolar musculature. It can decrease uterine motility and produce relaxation of uterine musculature without diminution of maternal and fetal arterial oxygen saturation. In the light of a century's experience under varied and difficult obstetrical situations, any other potent inhalational agent selected for obstetrical anesthesia should demonstrate some specific advantage in preference to the choice of ether. This obstetrical anesthetic agent has a high incidence of satisfactory results when skillfully administered to the properly prepared patient.

Ether was the first agent administered to achieve obstetrical anesthesia. Some of the Great Names in the progress of medicine are associated with the advent and use of ether as a means of producing anesthesia. Just to mention a few chronologically: Lullius discovered "sweet vitriol" (ether) in the thirteenth century; Paracelsus discovered its soporific action in the fifteenth century; Frobenius of the eighteenth century gave it the name of ether; Michael Faraday, a pupil of Humphry Davy, first suggested the anesthetic possibilities of ether in 1818. Both of the latter two eminent scientists working with Thomas Beddoes used ether in the treatment of painful respiratory conditions during the nineteenth century. John Snow, the first scientific anesthetist; James Young Simpson, the famous obstetrician; and, in America, Crawford W. Long, John Collins Warren, Oliver Wendell Holmes, Walter Channing, and a host of other great physicians of the nineteenth century were associated with the development and progress of ether anesthesia.

It is probably not necessary to remind this audience that the bust of the first physician to be placed in the Hall of Fame of Great Americans, on University Heights, was that of William Thomas Green Morton. One may read the following inscription on his bust:

"I leave it to surgeons and physicians to speak the praises of ether in the various operations in which it is now universally used whenever the relief of pain is an object of importance."

After more than a century of experience with ether this statement of Morton's still holds true.

During the preceding thirty-odd years the maternal mortality for the birth registration area of the United States has been reduced by 21 per cent. There were 6.1 maternal deaths per 1,000 live births in 1915. The rate for 1947 was 1.3. The neonatal death rate at the Boston Lying-in Hospital¹ during the past half century has been reduced by 66.6 per cent. The rate for infants weighing over five and one-half pounds was 5 in 1949. This achievement is due primarily to the practice of better obstetrics by physicians. The chief causes of deaths during that period were frequent use of high forceps, hemorrhage, operative trauma, poor preparation of the patient for delivery, poor obstetrical anesthesia when available, all adding up to shock and resulting in death. Other causes were other forms of "meddlesome obstetrics," eclampsia, puerperal infection. The development of better obstetrical anesthesia has contributed

greatly to the better and more conservative management of labor. The challenge of making the period of childbirth safer for mother and baby still exists for all interested physicians.

Summary and Conclusions

There is a modern trend toward appreciation of the fact that the selection of preanesthetic medication is dependent on the choice of agent and technique to be employed for obstetrical anesthesia. The dose and route, as well as the timing of administration of the selected premedicating drugs, are of importance. Paradoxical as it may seem, the deeper the anesthesia requirements of the obstetrical procedure are, the lighter the effects of the preanesthetic medication should be. The existing physiological alterations of the mother and her fetus, as well as the environment in which the labor is conducted, should determine the choice of obstetrical anesthesia. Experience teaches the prudent physician the futility of standardizing the anesthetic procedure to fit all obstetrical patients.

The trend of events in the clinical application of the more recent discoveries in physiology, biochemistry, pharmacology, and allied clinical disciplines to obstetrical anesthesia have been considered. Brief mention has been made of men and events, but emphasis was placed on the progress of concepts and ideas. We hope that this progress will continue under our system of free exchange of thought.

I should like to focus attention on another important modern trend, that of the growing importance of human relations. There exists the tendency in obstetrics and in other specialties of medicine of placing too much emphasis on the anesthetic drug or technique to be employed rather than on the training, experience, and judgment of the physician administering the anesthesia for the obstetrical patient. The progress in safeguarding the obstetrical patient is not reflected by the increase in the number of midwives but by the availability of the modern well-trained obstetrician. Similarly, the services of a physician well trained in the science and art of anesthesiology, as an integral part of medicine, will constitute a safeguard during the conduct of obstetrical anesthesia. The contributions of anesthesia to obstetrics are becoming increasingly recognized. The modern trends in obstetrics and anesthesia emphasize the need of exercising judgment, skill, and mutual confidence of the obstetrical team, composed of the obstetrician, the anesthesiologist, and their co-workers, if the lives of mother and baby are to be safeguarded during childbirth.

References

1. Irving, F. C.: *New England J. Med.* 244: 91, 1951.
2. Hershenson, B. B.: *New England J. Med.* 239: 429, 1948.
3. Reid, D. C., and Cohen, M. E.: *J. A. M. A.* 142: 615, 1950.
4. Javert, C. T., and Hardy, J. D.: *Anesthesiology* 12: 189, 1951.
5. Beecher, H. K.: *Anesthesiology* 12: 633, 1951.
6. Assali, N. S., and Prystowsky, H.: *J. Clin. Investigation* 29: 1354, 1950.
7. Orkin, L. R., and Rovenstine, E. A.: *M. Clin. North America* 35: 805, 1951.
8. Hershenson, B. B.: *Proc. Third American Congress on Obstetrics and Gynecology*, 1947, pp. 113-121.

HODGKIN'S DISEASE AND PREGNANCY

H. L. STEWART, JR., M.D., AND RAYMOND W. MONTGOMERY, M.D., DETROIT, MICH.

*(From the Departments of Obstetrics and Gynecology and Medicine,
the Henry Ford Hospital)*

THE unfavorable prognosis of Hodgkin's disease does not preclude pregnancy. Whether the fatal outcome is hastened by intercurrent pregnancy is a highly significant clinical question. The obstetrician and the internist are particularly interested in knowing whether the patient will be placed in greater jeopardy in the event of pregnancy and what effect the disease will have on the offspring. The capricious and variable course of Hodgkin's disease makes it difficult to appraise the influence of pregnancy. The rare concurrence of these two conditions emphasizes the importance of careful clinical surveys in order that speculations be reduced to a minimum.

There have been three women with Hodgkin's disease observed during four pregnancies at the Henry Ford Hospital during a period from 1940 to 1950. The important clinical features of these cases are presented in abstract. Review and analysis of the literature are included since our observations are not in complete agreement with previous surveys.

Case Reports

CASE 1.—(No. 284454) M. S., aged 23 years, presented herself at the Henry Ford Hospital in April, 1940, because of a swelling in the right side of the neck of several months' duration. She was otherwise asymptomatic. Biopsy of a right cervical node under local anesthesia demonstrated a histologic picture of Hodgkin's disease. The chest x-ray was negative. Complete regression of the enlarged right cervical lymph nodes followed the initial course of deep x-ray therapy in June, 1940.

The last menstrual period of her first pregnancy began April 20, 1940. The pregnancy progressed uneventfully and without clinical evidence of aggravation of the Hodgkin's disease. A normal, full-term, living female baby weighing 3,700 grams was delivered spontaneously on Jan. 12, 1941. The delivery was uncomplicated and blood loss was minimal. The postpartum course was afebrile and the patient breast fed her baby for six weeks. The child is now 11 years of age and shows no evidence of Hodgkin's disease.

In May, 1941, readmission to the hospital was necessary because of pain in the back and left hip. X-rays revealed an osteolytic lesion of the lower portion of the left ilium and fourth lumbar vertebra, interpreted as a metastatic lesion of Hodgkin's disease. Roentgen therapy afforded complete relief of pain.

She was readmitted because of occipital and cervical discomfort; metastatic involvement of the eighth cervical vertebra was noted. Although x-ray therapy was sufficient for relief of the pain, the patient presented numerous complaints including insomnia, anorexia, loss of energy, and general malaise.

The last menstruation of the second pregnancy began Oct. 1, 1941. Due to the poor general state of the patient as well as clinical and x-ray spread of the disease, the attending physician and several consultants favored the prevalent opinion that the pregnancy should be terminated. Interruption of the pregnancy on Dec. 12, 1941, apparently did not appreciably alter the course of the disease. Histological study of the products of conception failed to

reveal any evidence of Hodgkin's disease of the fetus or the placenta. Several months later a course of deep x-ray therapy over the lower abdomen was followed by permanent amenorrhea. Although the patient showed some symptomatic improvement, the downward trend of the disease continued with death four and one-half years later. Necropsy revealed Hodgkin's disease involving the mediastinal lymph nodes, upper lobe of the left lung, gastric lymph nodes, and peripancreatic tissue, spleen, and retroperitoneal lymph nodes.

CASE 2.—(No. 476390) M. H., aged 25 years, was hospitalized on May 22, 1946, for delivery of a full-term, living male baby, weighing 3,210 grams. Physical examination revealed no evidence of Hodgkin's disease. The puerperium was normal.

On April 28, 1947, she was examined in the Nose and Throat Division because of a swelling in the right side of the neck which was noted while feeding the baby, then 11 months of age. She believed this painless lump had been present during the last four months, but came for examination only at the insistence of her family. On examination there was a nontender, discrete mass approximately 8 cm. in diameter with several smaller masses in the right supraclavicular area. No other significant physical findings were in evidence. Chest x-ray revealed a rounded mass extending into the upper right mediastinum. Biopsy of a cervical node on May 9, 1947, presented a typical microscopic picture of Hodgkin's disease (Fig. 1).

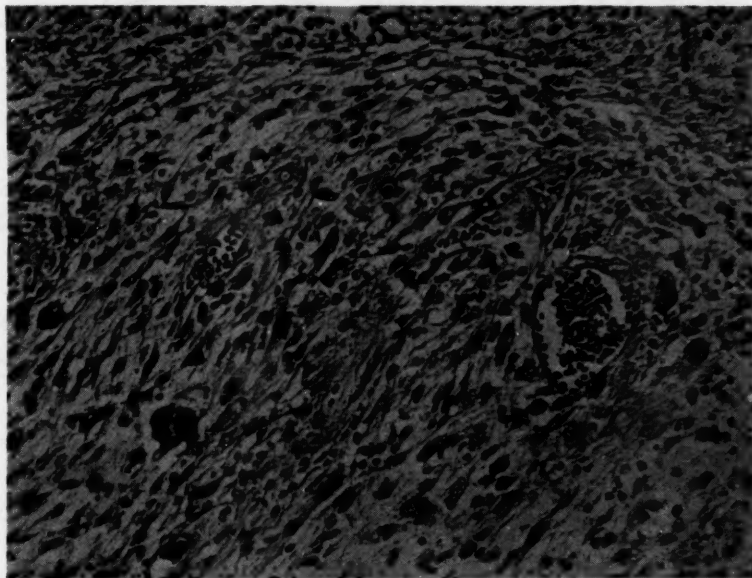


Fig. 1.—Biopsy of a cervical node presented a typical microscopic picture of Hodgkin's disease (M. H., Case 2).

The patient received deep x-ray therapy, 700 r to the right cervical area and 1,400 r to the hilar area of the lungs. Additional roentgen therapy for the Hodgkin's disease has not been required.

Subsequent visits revealed the patient to be asymptomatic. Her appetite was excellent and she weighed 103½ pounds. There were no symptoms referable to the cardiorespiratory or gastrointestinal system. The menstrual cycle was regular and normal.

The patient returned Jan. 31, 1950, for prenatal care, stating that the last menstrual period began Nov. 25, 1949. The antepartum course was uneventful and there was no clinical evidence of activity of the Hodgkin's disease. The patient weighed 132 pounds at the time of spontaneous delivery of a full-term, living male baby weighing 2,910 grams on Sept. 4, 1950. Blood loss was not excessive. Microscopic examination of the placenta was normal. Lactation was successful and the baby was breast fed for several months. The postpartum temperature was normal and the patient was discharged from the hospital in good condition.

on the seventh postdelivery day. Chest x-ray on Sept. 19, 1950, was negative. Periodic examinations have detected no activity of the Hodgkin's disease. The clinical course of the disease relative to the hemoglobin, temperature, and weight changes are graphically shown in Fig. 2. Pregnancy and lactation had no apparent effect on the course of the disease.

CASE 3.—(No. 531540) V. J. was 25 years of age when she entered this hospital in February, 1948, because of a swelling in the right side of the neck of 8 months' duration. Biopsy of one of the larger masses in the neck revealed Hodgkin's disease of the granulomatous type. The clinical course was a recurrent febrile type with visceral organ involvement including hepatomegaly. Several courses of deep x-ray therapy were given to the cervical, axillary, and mediastinal nodes.

HODGKIN'S DISEASE AND PREGNANCY.

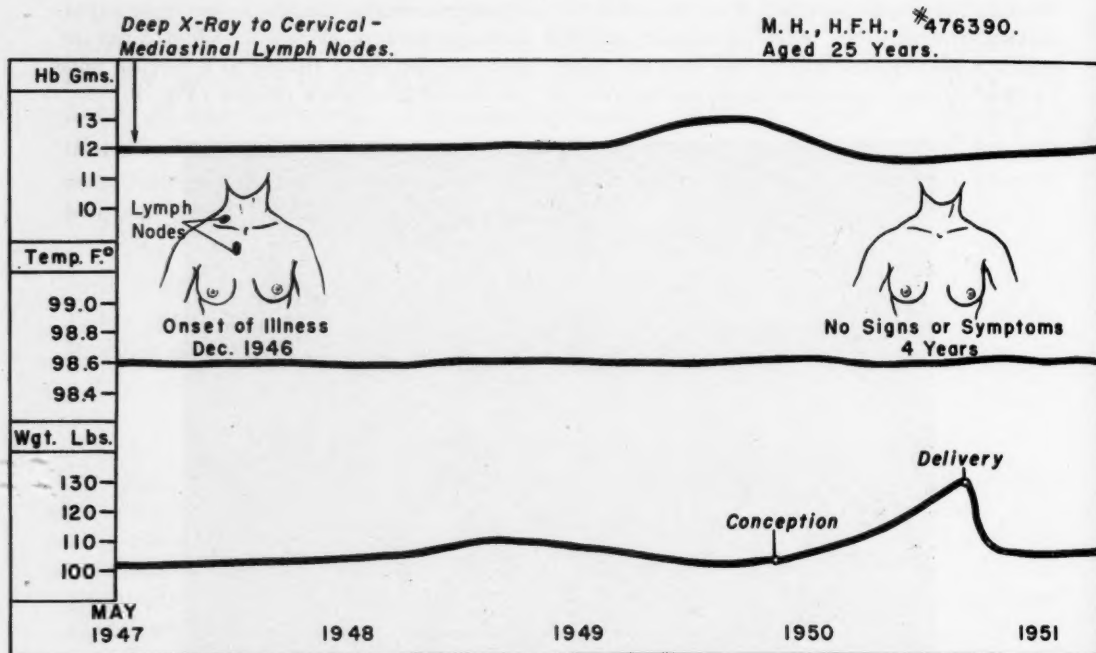


Fig. 2.—The clinical course of Hodgkin's disease and pregnancy relative to the hemoglobin, temperature, and weight changes is graphically shown. Pregnancy and lactation had no apparent effect on the course of the disease.

Menstruation continued rhythmically every 28 days with the last menstruation beginning Dec. 26, 1948. The general condition of the patient during pregnancy was not good even though there was no progression of the lymphadenopathy. Daily temperature elevations ranged from normal to 100° F. (Fig. 3).

The weight at the time of the conception was 112 pounds which steadily decreased to 106 pounds at the time of delivery. Pregnancy terminated spontaneously at eight and one-half months after a four and one-half hour labor assisted by low forceps delivery and midline episiotomy. A female baby weighing 2,330 grams was normal except for a mild talipes equinovarus. Gross and microscopic examination of the placenta revealed no evidence of any specific lesion or inflammatory change. Lactation was not attempted due to the poor general state of the patient.

Immediately post partum, daily temperature elevations ranged from normal to 103° F. The pelvic organs showed no physical signs of infection. The temporary temperature elevations were manifestations of the Hodgkin's disease. She responded poorly to blood trans-

fusions, nitrogen mustard, and deep x-ray therapy. Response to ACTH and triethylene melamine have not been encouraging. Following this temporary improvement the patient's course has deteriorated progressively. The clinical course of the disease, relative to the hemoglobin, temperature, and weight changes, is graphically illustrated in Fig. 3 and shows no significant alteration with the occurrence of an intercurrent pregnancy. The wider fluctuations of the hemoglobin and temperature curves are due to the more frequent determinations during the several postpartum hospital admissions. Suppression of menstruation followed the last course of the deep x-ray over the lower abdomen. The patient remains alive at this time with the responses to various agents producing shorter remissions. The condition of the baby is excellent.

HODGKIN'S DISEASE AND PREGNANCY.

V.J., H.F.H., # 531540
Aged 23 Years.

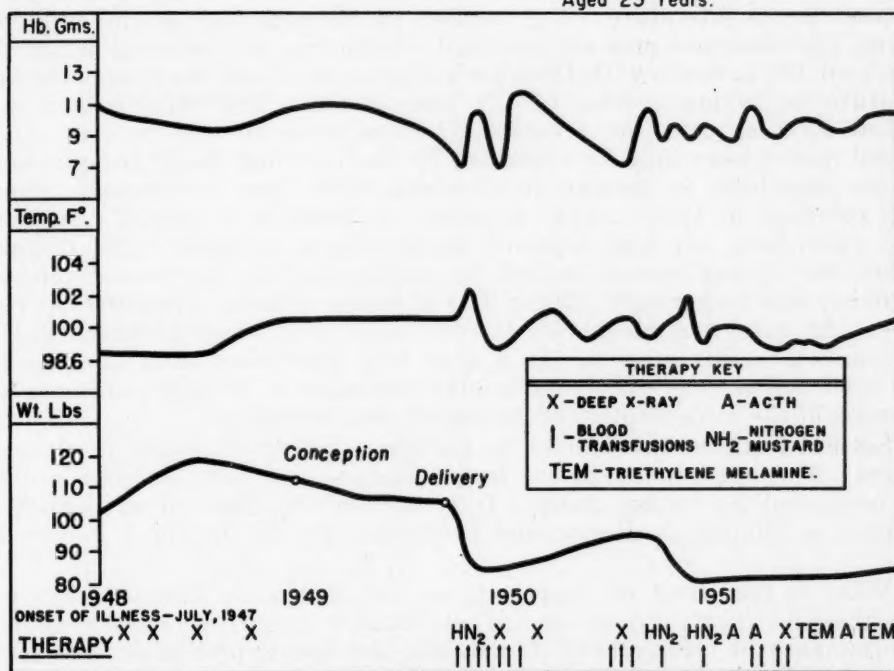


Fig. 3.—There was no significant alteration of the hemoglobin, temperature, and weight curves with the occurrence of intercurrent pregnancy in Hodgkin's disease.

Comment

The incidence of pregnancy complicating Hodgkin's disease is difficult to estimate accurately. The three cases discussed above were treated at this institution from 1940 to 1950. There were 18,509 deliveries during this ten-year period which represents an incidence of one case in 6,100 deliveries. In this respect, our statistics support the findings of a 12-year study by Palacios Costa, Chavanne, and Zebel,³⁰ who reported five cases of Hodgkin's disease in 30,000 gestations, or an incidence of one case in 6,000 deliveries. The rare occurrence of the two conditions is at once apparent and may in part account for the divergence of opinions as to the influence of pregnancy.

During the interval of 1940 to 1950, Hodgkin's disease was diagnosed in this hospital among 35 males and 21 females. Only six of the affected females were married and in the childbearing age. One of these received roentgen therapy over the lower abdomen shortly after the diagnosis was made, result-

ing in amenorrhea. Two cases were seen only in consultation and during the initial x-ray treatment without further clinical observation. Management and course of the three remaining women during their pregnancies are a part of this review.

Our review of the literature as to the number of accepted cases of Hodgkin's disease and pregnancy is conspicuous by the lack of agreement with previous surveys. Kasdon⁴¹ reviewed this problem in 1949, with a report of three cases and a discussion of 29 acceptable cases from the literature. In 1951, Tenenblatt and Horton⁴⁷ added a case report and acknowledged only 33 cases in the literature. In the same year, McSwain and Haber⁴⁸ reported 67 women with Hodgkin's disease and pregnancy with delivery of 60 normal babies.

Table I is a tabulation of our summary of cases of Hodgkin's disease recorded in the literature. The number of cases as well as the total pregnancies and their outcome are recorded. Including our personal series, there have been 109 patients with Hodgkin's disease who have been reported in the literature as having a total of 134 pregnancies. This represents a rather marked increase over the accepted 67 cases prior to this review. Such a marked discrepancy may be explained by the fact that many acceptable case reports, especially in foreign publications, have been overlooked. Several cases recorded in Table I have appeared in journals of limited distribution. Many cases have not been reported specifically as pregnancy and Hodgkin's disease, but appear as case reports in publications on the general subject of pregnancy and malignancy. Regardless of where or under what title the report occurs, the case was acceptable if reasonable proof the concurrence of the two conditions was present. It is true that obstetrical data in some cases were brief and sketchy due to the lengthy discussion of Hodgkin's disease to the exclusion of the mere mention of pregnancy and its outcome.

Several authors have failed to include a biopsy diagnosis in their case reports. The clinical discussion leaves little doubt that Hodgkin's disease was confirmed by biopsy study. It is our opinion that all authentic cases accepted as Hodgkin's disease and pregnancy should include a biopsy diagnosis.

What is the effect of pregnancy on the Hodgkin's disease? For many years this all-important question has continued in a controversial state. Should the pregnancy be terminated? If not, will the disease process be accelerated? Herz,⁹ Dyes,¹⁰ and Blitz¹⁵ advocated termination of pregnancy in the presence of Hodgkin's disease. Gemmell³ recommended termination of pregnancy "when early Hodgkin's disease and early pregnancy occur together. If Hodgkin's disease is advanced, the termination of pregnancy would probably be too late, and if the pregnancy is far advanced it is likely that the outlook in an artificially produced puerpera would be no better than if the patient were allowed to go to term." Even though the recent reviews of Kasdon,⁴¹ Bichel,⁴³ Tenenblatt and Horton,⁴⁷ and McSwain and Haber⁴⁸ do not advocate interruption of pregnancy, the maternal death as reported by Portmann and Mulvey⁴⁴ no doubt influenced their decision that "pregnancy may result in exacerbation of Hodgkin's disease."

The unpredictable clinical course of Hodgkin's disease makes it quite difficult to interpret properly acute exacerbations and remissions in relation to the presence of pregnancy. Acute exacerbations occur without premonitory signs and may occur during or following a pregnancy without necessarily having any direct relation to the presence of pregnancy. It is important to recognize that the degree of malignancy and general nutritional state of the patient as well as the length of spontaneous remissions and response to roentgen therapy

TABLE I. HODGKIN'S DISEASE AND PREGNANCY

			CASES	PREG- NANCIES	TERMINATION OF PREGNANCY			
					ABORTION		PRE- MATURE	FULL TERM
					SPON- TANEOUS	INDUCED		
1.	1911	Davis, A. B.	1	1	0	0	0	1
2.	1921	Bowing, H. H.	Insufficient data					
3.	1923	Gemmel, A. A.	1	3	1	0	0	2
4.	1926	Priesel and Winkelbauer	1	1	0	0	0	1
5.	1931	Debiasi	1	1	0	0	0	1
6.	1932	Paviot, Levrat and Jarrirot	1	1	0	0	0	0
7.	1932	Pallasse, M. M., Rheuter and Sauty	2	2	0	0	1	1
8.	1933	Minciotti	1	1	0	0	0	1
9.	1934	Herz, Albert	5	5	0	0	0	5
10.	1934	Luetkens	1	1	0	0	0	1
11.	1935	Bastenie, Sluys and Snoeck	1	1	0	0	0	1
12.	1935	Morosi	2	2	0	0	0	2
13.	1936	Darling	1	1	0	0	0	0
14.	1938	V. Braitenberg	1	1	0	0	0	1
15.	1937	Blitz	2	2	0	2	0	0
16.	1939	Baltzer, H.	1	2	1	0	0	1
17.	1939	Salvini, A.	1	1	0	0	0	1
18.	1939	Horster, H.	1	2	0	1	0	1
19.	1939	Dyes, O.	2	2	0	0	0	2
20.	1930	Adair, F. L.	2	4	1	1	0	2
21.	1940	dePalo	1	1	0	0	1	0
22.	1941	Kushner, J. I.	1	1	0	0	0	1
23.	1941	Heynemann, T.	1	1	0	0	0	1
24.	1942	Klawans, A. H.	1	1	0	0	0	1
25.	1942	Parade, G. W.	1	1	0	0	0	1
26.	1943	Fabian, D.	Thesis unavailable in U. S.					
27.	1944	Ludin, M.	3	3	0	0	0	3
28.	1945	Perrier, H.	5	8	1	1	0	6
29.	1945	Gilbert, R.	6	10	0	0	0	10
30.	1945	Palacios Costa N., Chavanne, F. C., and Zebel Fernandez, O.	5	5	0	0	0	5
31.	1945	Goldman, L. B., and Victor, A. W.	11	12	1	3	0	8
32.	1946	Wolff, J. R., and Limarzi, L. R.	2	2	0	0	0	2
33.	1946	Vayssiére, Dieulangard, and Lapeyre	1	1	0	0	1	0
34.	1947	Olmsted, G. S.	1	3	0	0	0	3
35.	1947	Jackson and Parker	3	3	0	1	0	2
36.	1947	Erf, L. A.	1	1	0	1	0	0
37.	1947	Nikischin, I. F.	3	3	2	0	0	1
38.	1948	Summers, J. E., and Reid, W. C.	1	2	0	0	1	1
39.	1949	Brougher, J. C.	1	1	0	0	0	1
40.	1949	Verhagen, A.	1	1	0	0	0	1
41.	1949	Kasdon, S. C.	3	3	0	1	1	1
42.	1949	Falsia, M. V., and Etala, F.	1	1	0	0	0	1
43.	1950	Bichel, J.	11	16	3	1	1	10
44.	1950	Portmann, W. V., and Mulvey, B. E.	4	6	0	0	0	5
45.	1950	Mertens, W.	4	4	0	0	0	4
46.	1950	van der Werff, J. T.	3	3	0	0	0	3
47.	1951	Tenenblatt, W., and Horton, C.	1	1	0	0	0	1
48.	1951	McSwain and Haber	2	2	0	0	0	2
49.	1951	Stewart and Monto	3	4	0	1	0	3
Total			109	134	10	13	6	101
			Maternal deaths				4	

are the important factors influencing the course of the disease. Acute exacerbations and long remissions have occurred during pregnancy and immediately post partum. It is difficult to state whether any one particular patient who goes through pregnancy will die sooner than she would otherwise have done.

Our review of the literature of 134 pregnancies substantiates the opinion that pregnancy does not exert a favorable or unfavorable influence on the general progression of the disease. No aggravation of the Hodgkin's disease was evident in the three pregnancies going to term in our series. Our observations are in agreement with those of others who believe that from an obstetrical point of view the pregnancy, parturition, and puerperium continue in an uncomplicated course in the majority, and that acute exacerbation of the disease is not more frequent during pregnancy than could be expected spontaneously. Termination of pregnancy, therefore, is not indicated.

It has been repeatedly stated in previous reviews that maternal deaths due to Hodgkin's disease have not occurred during pregnancy. In view of these reports, one might erroneously assume that there is a protective action during pregnancy whereby these patients do not die. We have found four maternal deaths due to Hodgkin's disease during pregnancy. Paviot, Levrat, and Jarriocot⁶ reported the first maternal death in 1932. In 1936, Darling¹³ reported the death of a patient with Hodgkin's disease during the second pregnancy. Following delivery of her first baby, the diagnosis of Hodgkin's disease was established by biopsy of an axillary lymph node. Later she was admitted for treatment of a metastatic lesion of the seventh cervical vertebra and died undelivered during the seventh month of gestation. Bichel⁴³ and Portmann and Mulvey⁴⁴ each had a death in their series bringing the total to four. This represents a maternal mortality of 2.9 per cent. Although 2.9 per cent is higher than the average maternal mortality, this figure is much lower than the expected mortality from leukemia or lymphosarcoma and other similar major complications of pregnancy.

Since the general consensus is that pregnancy does not adversely affect the course of Hodgkin's disease, a consideration of the reciprocal relations of these two conditions leads to the question of the effect of the disease on pregnancy.

It is apparent that the degree of malignancy may influence the decision of the patient regarding marriage. Most opinions advocate discouraging marriage and pregnancy because of the ultimate fatal termination of the disease. As stated by Gilbert,²⁹ "these events occur in spite of us." Whether fertility is impaired in Hodgkin's disease remains unanswered due to the lack of sufficient statistics. The fact, however, that there is a high incidence of multiparas in the cases in our review tends to refute the implication of infertility. The extent of the disease and its effect on the general health of the individual is the important factor influencing the fertility state even though there are no cases reported at autopsy where there was direct involvement of the ovaries and genital tract. Complete autopsy of our Case 3 did not show any genital-system involvement. Even though the uterus or ovaries are not directly involved many patients are eliminated as prospective mothers when roentgen therapy is applied over the lower abdomen leading to amenorrhea.

If the patient with Hodgkin's disease becomes pregnant, active therapy should be administered by x-ray as the indication arises, with adequate shielding and protection of the fetus in utero. The incidence of spontaneous abortion does not exceed the expected incidence among a large series of normal pregnant women. Tietze⁴⁰ reported spontaneous abortion as 7.0 per cent among 1,479 women of all age groups. Spontaneous abortion in women with Hodgkin's disease of all age groups, irrespective of parity, was 11 of 134 pregnancies or 8.2 per cent (Table I). Prematurity is not increased as only 6 of 134 pregnancies terminated prematurely.

Hodgkin's disease has been stated to lie pathogenetically on a divide which separates neoplasms and inflammations, being a tumor by its physical

signs and an inflammation by its general and hematological characteristics. While the etiology of Hodgkin's disease is unknown, it has been speculated that the agent producing this illness may be a "tumor virus" or an infective organism. If this hypothesis is true, one might expect to find a significant incidence of Hodgkin's disease in the offspring of mothers so afflicted.

The placenta is a highly protective organ to the offspring and this is one of the seldom-mentioned functions of the placenta. From 1866 to 1950, Bender⁵⁰ found only nine metastases of maternal tumors to the products of conception. In six cases the placenta was involved without harm to the baby, and in only two cases did the baby develop the maternal tumor without evidence of placental involvement. There is only one case on record where both baby and placenta showed evidence of the maternal tumor.

There is only one case on record accepted as transmission of Hodgkin's disease during intrauterine life as a true instance of congenital transmission.⁴ There was no placental study to verify the case as unquestionably transplacental transmission. The baby died of Hodgkin's disease at 3½ months of age. Since there are no cases on record of placental involvement of Hodgkin's disease, it serves to emphasize the importance of including placental studies in all cases of malignancy and pregnancy. The placental studies in our four pregnancies showed no evidence of Hodgkin's disease. The conspicuous absence of intrauterine transmission of the disease to the fetus favors the neoplastic etiology of Hodgkin's disease rather than the "tumor virus" theory.

The statement of Portmann and Mulvey that "the future of the offspring is not predictable" is not wholly supported from the findings of our review. Among the 121 pregnancies there were 10 spontaneous abortions, 2 stillbirths and 4 maternal deaths. A total of 105 living babies were delivered (86.7 per cent). These results favor the view that the chances for a living baby are not altered by any unfavorable influence of the disease on the pregnancy.

There is very little mention in the literature concerning lactation. Earlier reports avoided the issue mainly due to the lack of sufficient cases to form any conclusions as to the effects of lactation on the offspring. Nursing has not been generally advocated due to unknown etiology and transmission of the disease. Recent emphasis on the milk factor introduces further question.

There have been 17 mothers who breast fed their babies, including two of our personal observations. Not one breast fed baby has shown untoward effects or evidence of Hodgkin's disease. That lactation is detrimental to the well-being of either the mother or baby has not been substantiated by those mothers who nursed. It is our opinion that a mother should be permitted to nurse her baby unless it is quite obvious to the attending physician that the malignant manifestations of the disease are such that lactation is not in the best interests of the patient. It was for this reason that Case 3 of our series was not permitted to nurse.

Conclusion

Although previous reports have recorded less than half the number, a careful review of the literature revealed 109 women with 134 pregnancies complicating Hodgkin's disease. Analysis of these cases, which includes four pregnancies from our series, furnishes the basis for the following conclusions:

1. The woman with Hodgkin's disease is not necessarily infertile.
2. Pregnancy complicating Hodgkin's disease is not an indication for therapeutic termination.
3. Obstetrically, the majority of women with Hodgkin's disease do well during pregnancy, parturition, and the puerperium.

4. The clinical course of Hodgkin's disease is neither favorably nor unfavorably influenced by pregnancy. Acute exacerbations of Hodgkin's disease may occur during pregnancy but are no more frequent than would be expected spontaneously.

5. Four maternal deaths from Hodgkin's disease have occurred during pregnancy.

6. Evidence of transplacental transmission of the disease was lacking. There is only one case in the literature of intrauterine transfer of Hodgkin's disease from mother to baby. This evidence favors the neoplastic theory of Hodgkin's disease.

References

1. Davis, A. B.: *Bulletin Lying-In Hospital*, N. Y. 7: 151, 1911.
2. Bowing, H. H.: *Surg. Clin. North America* 1: 1327, 1921.
3. Gemell, A. A.: *J. Obst. & Gynaec. Brit. Emp.* 30: 373, 1923.
4. Priesel, A., and Winkelbauer, A.: *Virchows Arch. f. path. Anat.* 262: 749, 1926.
5. Debiasi, E.: *Folia gynaec.* 28: 167, 1931.
6. Paviot, J., Levrat, M., and Jarricot, H.: *Lyon méd.* 150: 437, 1932.
7. Pallasse, M. M., Rheuter and Santy: *Lyon méd.* 150: 531, 1932.
8. Minciotti, G.: *Gior. veneto di sc. med.* 6: 515, 1933.
9. Herz, Albert: *Wien. Arch. f. inn. Med.* 24: 427, 1934.
10. Luetkens: *Dissertation*, Freiburg, 1934. Quoted by von Braitenberg.¹⁴
11. Bastenie, P., Sluys, and Snoeck: *Bruxelles-méd.* 16: 290, 1935.
12. Morosi, G.: *Riv. ital. di ginec.* 18: 329, 1935.
13. Darling, M. A.: Quoted by G. S. Olmsted.³⁴ Personal communication.
14. von Braitenberg, H.: *Beitr. z. path. Anat. u. allg. Path.* 101: 301, 1938.
15. Blitz: *Frankfurt a.m. 1937, Inaug.-Dissertat.* Quoted by G. W. Parade.²⁵
16. Baltzer, H.: *Zentralbl. f. Gynäk.* 63: 2129, 1939.
17. Salvini, A.: *Ginecologia* 5: 226, 1939.
18. Horster, H.: *Deutsche med. Wehnschr.* 65: 680, 1939.
19. Dyes, O.: *München. med. Wehnschr.* 86: 605, 1939.
20. Adair, F. L.: *Obstetric Medicine*, Philadelphia, 1940, Lea & Febiger, vol. 2, p. 610.
21. dePalo: *Clin. ostet.* 42: 477, 1940.
22. Kushner, J. I.: *AM. J. OBST. & GYNEC.* 42: 536, 1941.
23. Heynemann, T.: *Zentralbl. f. Gynäk.* 65: 1918, 1941.
24. Klawans, A. H.: *AM. J. OBST. & GYNEC.* 43: 895, 1942.
25. Parade, G. W.: *Deutsche med. Wehnschr.* 66: 375, 1940.
26. Fabian, D.: *Thèse de Halbe*, 1943. Quoted by Rene Gilbert.²⁹
27. Ludin, M.: *Strahlentherapie* 74: 367, 1944.
28. Perrier, H.: *Schweiz. med. Wehnschr.* 75: 1014, 1945.
29. Gilbert, R.: *Schweiz. med. Wehnschr.* 75: 53, 1945.
30. Palacios Costa, N., Chavanne, F. C., and Zebel Fernandez, O.: *An. de ateneo*, Buenos Aires, 127, 1945.
31. Goldman, L. B., and Victor, A. W.: *New York State J. Med.* 45: 1313, 1945.
32. Wolff, J. R., and Limarzi, L. R.: *AM. J. OBST. & GYNEC.* 51: 447, 1946.
33. Vayssiére, Dieulangard, and Lapeyre: *Gynéc. et obst.* 45: 634, 1946.
34. Olmsted, G. S.: *The Grace Hosp. Bull.* 25: 27, 1947.
35. Jackson, H., Jr., and Parker, F., Jr.: *Hodgkin's Disease and Allied Disorders*, New York, 1947, Oxford University Press, p. 91.
36. Erf, L. A.: *Am. J. Clin. Path.* 17: 268, 1947.
37. Nikischin, I. F.: *Geburtsh. u. Frauenh.* 7: 110, 1947.
38. Summers, J. E., and Reid, W. C.: *J. A. M. A.* 137: 787, 1948.
39. Brougher, J. C.: *West. J. Surg.* 57: 430, 1949.
40. Verhagen, A.: *Strahlentherapie* 79: 127, 1949.
41. Kasdon, S. C.: *AM. J. OBST. & GYNEC.* 57: 282, 1949.
42. Falsia, M. V., and Etala, F.: *Bol. Soc. de obst. y ginec. de Buenos Aires* 28: 375, 1949.
43. Bichel, J.: *Acta radiol.* 33: 427, 1950.
44. Portmann, W. V., and Mulvey, B. E.: *Cleveland Clin. Quart.* 17: 149, 1950.
45. Mertens, W.: *München. med. Wehnschr.* 23: 933, 1950.
46. van der Werff, J. T.: *Acta radiol.* 33: 31, 1950.
47. Tenenblatt, W., and Horton, C.: *West. J. Surg.* 59: 120, 1951.
48. McSwain, B., and Haber, A.: *South. M. J.* 44: 105, 1951.
49. Tietze, C.: *J. A. M. A.* 142: 1348, 1950.
50. Bender, S.: *Brit. Med. J.* 1: 980, 1950.

FURACIN VAGINAL SUPPOSITORIES IN PRE- AND POSTOPERATIVE TREATMENT OF CERVIX AND VAGINA*

JEROME SCHWARTZ, M.D., LYNBROOK, N. Y.

(From the Department of Obstetrics and Gynecology, Fordham Hospital)

THE problem of correctly treating the postoperative cervix and vagina is a highly controversial one. The methods of treatment are numerous and varied. Many therapeutic measures and drugs are in popular usage today, including tampons, suppositories, powders, jellies, creams, douches, sulfonamide drugs, and penicillin. This multiplicity of therapeutic agents suggests that the best treatment for the postoperative cervix and vagina has not yet been found.

Many conditions exist which require correction in order to facilitate and hasten postoperative healing of the cervix and vagina (Marbach,¹ Slater²). Postoperatively, (1) the pH of the vagina approaches neutrality or alkalinity; (2) the vaginal flora changes from Grade 1 to Grades 2 and 3 (Schottmüller,³ Rakoff⁴); (3) the availability of the tissue glycogen is decreased due to tissue destruction. These conditions favor the growth of secondary bacterial invaders with a concomitant decrease in the healing propensities of the postoperative cervix and vagina. In order to restore the vagina to a normal physiological balance, it is essential to depress the secondary bacterial invaders, since it is principally these saprophytic organisms which are responsible for these disturbances.

As Furacin (brand of nitrofurazone, New and Nonofficial Remedies) is bactericidal to the majority of bacteria found in vaginal infections, it was decided to utilize Furacin in a vaginal suppository for the pre- and postoperative treatment of the cervix and vagina (Table I).

Furacin is not bactericidal to Döderlein's bacillus (vaginal strain of *Lactobacillus acidophilus*). Its action is not seriously inhibited in the presence of such organic matter as blood, serum, and bacterial debris (Dodd⁵).

Furacin vaginal suppositories contain Furacin 0.2% dissolved in a self-emulsifying, water-miscible base composed of glyceryl laurate 10% and a synthetic water-dispersible wax 89.8%. In the vagina, the suppositories melt within 10 to 15 minutes, mix freely with the aqueous vaginal secretions to form a creamy emulsion and spread uniformly over the cervix and vagina. The effectiveness of the suppository is retained for at least 6 to 8 hours.

Material and Results

Furacin vaginal suppositories were used in 90 cases. In almost all instances a routine method for the use of the suppositories was utilized for each of the various operative procedures. The operations performed are outlined in Table II.

*The Furacin Vaginal Suppositories were supplied by Eaton Laboratories, Norwich, New York.

TABLE I. THE ANTIBACTERIAL SPECTRUM OF FURACIN IN VITRO*
(Bactericidal Concentration in Milligrams per 100 c.c. of Broth)

GRAM-NEGATIVE		GRAM-POSITIVE	
<i>Aerobacter aerogenes</i>	4.0	<i>Bacillus anthracis</i>	1.0
<i>Brucella abortus</i>	1.0	<i>Bacillus subtilis</i>	0.5
<i>Brucella melitensis</i>	10.0	<i>Clostridium histolyticum</i>	1.0
<i>Chromobacterium violaceum</i>	0.5	<i>Clostridium novyi</i>	2.5
<i>Escherichia coli</i>	1.25	<i>Clostridium perfringens</i>	20.0
		(<i>B. welchii</i>)	
<i>Hemophilus pertussis</i>	20.0	<i>Clostridium septicum</i>	1.0
<i>Klebsiella pneumoniae</i>	2.0	<i>Clostridium sporogenes</i>	10.0
<i>Neisseriae catarrhalis</i>	5.0	<i>Clostridium tetani</i>	20.0
<i>Neisseriae gonorrhoeae</i>	1.0	<i>Corynebacterium diphtheriae</i>	4.0
<i>Neisseriae meningitidis</i>	2.5	<i>Corynebacterium xerose</i>	20.0
(intracellularis)			
<i>Proteus morganii</i>	10.0	<i>Diplococcus pneumoniae</i>	6.6
<i>Proteus vulgaris</i>	10.0	<i>Gaffkya tetragena</i>	20.0
		<i>Micrococcus (Staphylococcus)</i>	1.0
<i>Salmonella enteritidis</i>	1.0	<i>pyogenes</i> var. <i>albus</i>	
<i>Salmonella paratyphi</i>	1.0	<i>Micrococcus (Staphylococcus)</i>	1.25
		<i>pyogenes</i> var. <i>aureus</i>	
<i>Salmonella schottmuelleri</i>	1.0	<i>Mycobacterium tuberculosis</i>	20.0
<i>Salmonella (Eberthella)</i>	1.0	(var. <i>hominis</i>)	
<i>typhosa</i>		<i>Mycobacterium tuberculosis</i>	20.0
<i>Serratia marcescens</i>	6.6	(H37Rv)	
		<i>Streptococcus faecalis</i>	20.0
<i>Shigella dysenteriae</i>	1.0	<i>Streptococcus pyogenes</i>	10.0
<i>Shigella paradysenteriae</i>	0.8	(hemolyticus)	
		<i>Streptococcus mitis (viridans)</i>	10.0

*Personal communication from Eaton Laboratories.

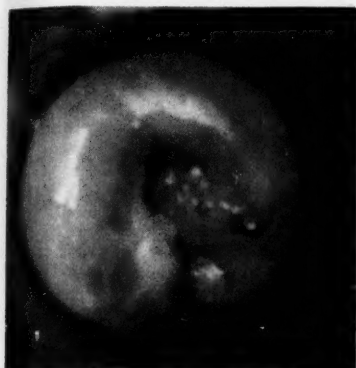
TABLE II. OPERATIVE PROCEDURES PERFORMED

	TEST GROUP, FURACIN VAGINAL SUPPOSITORIES USED POSTOPERATIVELY		CONTROL GROUP
Cervical operations	39		34
Cauterization of cervix		32	28
Conization of cervix		3	4
Amputation of cervix		2	1
Cervical polypectomy		2	1
Vaginal operations	25		23
Anterior-posterior colporrhaphy		14	14
Fothergill-Manchester procedure		8	9
Vaginal hysterectomy		3	0
Total abdominal hysterectomy	23		19
Radium treatment of cervix for carcinoma	3		3

Postelectrosurgical Treatment of Cervix (32 Patients)

Those patients requiring electrocauterization or conization of the cervix were all treated postoperatively in the same manner. The method of electrocauterization, however, varied in that the spark-gap cautery, the hot electrode cautery, and the radio-frequency cauterodyne were utilized.

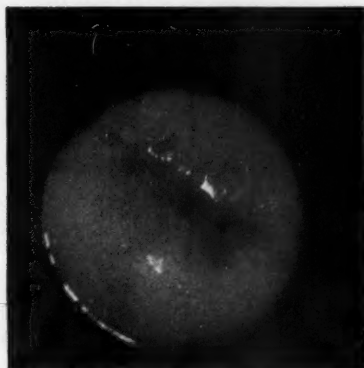
Routine: Without any preparatory treatment, the cervix is cauterized in a radial wheel-spoke fashion. A Furacin vaginal suppository is inserted into the vaginal canal and held in place with a vaginal tampon. The tampon is removed the next morning and the patient takes a vinegar douche (4 tablespoons of white vinegar to 2 quarts of warm water). Following the douche a Furacin suppository is inserted into the vagina. This procedure is performed



A. Pre-cauterization.

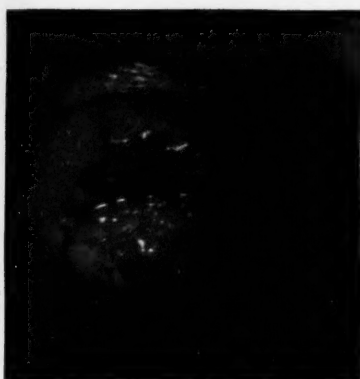


B. 2 days post-cauterization.

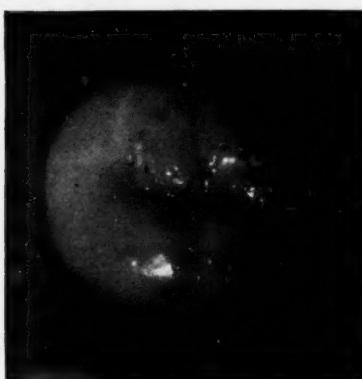


C. 3 weeks post-cauterization.

Fig. 1.—E. K., 35-year-old, para iii, grav. iii, with history of vaginal discharge of 7 months' duration. Examination revealed hypertrophied cervix with marked erosion.



A. Pre-cauterization.

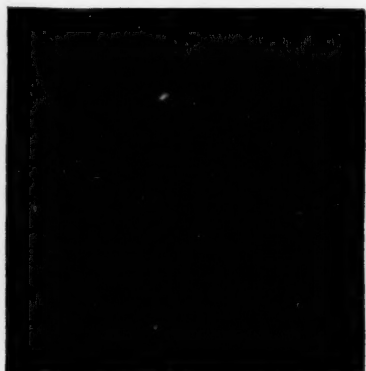


B. 2 weeks post-cauterization.

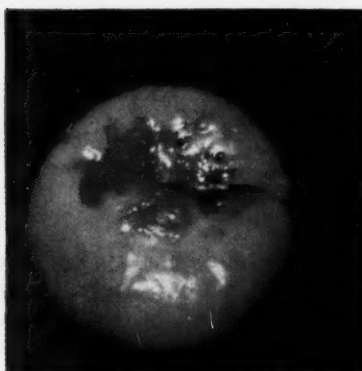


C. 3 weeks post-cauterization.

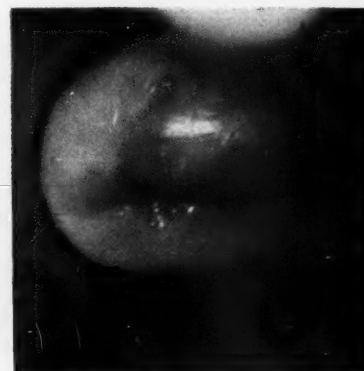
Fig. 2.—M. C., 40-year-old, para ii, grav. ii, with history of malodorous discharge. Examination revealed marked cervical erosion about the external os.



A. Pre-cauterization.



B. 11 days post-cauterization.



C. 3½ weeks post-cauterization.

Fig. 3.—E. J., 28-year-old, para iii, grav. iii. Routine examination revealed marked erosion of the posterior lip of the cervix.

twice daily, once in the morning and again in the evening. The patient is seen at weekly intervals. During the period of treatment she is cautioned to refrain from sexual intercourse. If menstruation occurs during the course of treatment, the douches are discontinued but the suppositories are still inserted twice daily.

All cervixes healed rapidly and cleanly without any discomfort. Most healed in 2 weeks and all were healed within 3 weeks (Figs. 1 and 3). In no instance did cervical stenosis develop, although routine postcauterization dilatations of the cervix were not performed. No cases of postcauterization bleeding were noted.

With the use of Furacin vaginal suppositories it was noted, as compared to results obtained with former types of treatment, that (1) healing time was accelerated; (2) the incidence of postcauterization infection and bleeding was reduced to zero; and (3) the slough and malodorous discharge from the vagina were markedly decreased.

Vaginal Operations (25 Patients)

Routine.—For two days prior to operation, Furacin vaginal suppositories are inserted into the vagina twice daily. A vinegar douche is given on the morning of the operation to cleanse the vagina of remnants of the suppository. Forty-eight hours following operation, after the packing is removed, one Furacin vaginal suppository is inserted into the vagina daily until the patient leaves the hospital.

In this group it was also observed that Furacin vaginal suppositories (1) caused more rapid healing; (2) decreased postoperative infection; (3) reduced the amount and odor of vaginal discharge, and (4) removed the "irritating" feeling usually experienced by patients following vaginal operations.

The patients were permitted out of bed on the third or fourth day and were discharged on the eighth to tenth day.

Total Abdominal Hysterectomy (23 Patients)

Routine.—Twenty-four to forty-eight hours prior to operation, a Furacin vaginal suppository is inserted into the vagina twice daily. On the morning of operation, a vinegar douche is used to cleanse the vagina of any remnants of the suppository. Twenty-four hours postoperatively, the patient is started on one Furacin vaginal suppository daily which is continued for the duration of her hospital stay.

Results.—The vaginal vault was well healed in 6 to 8 days, with a noticeable decrease in the postoperative vaginal bloody discharge.

Because of its wide bactericidal spectrum, Furacin vaginal suppositories placed in the vagina prior to hysterectomy prevent infection of the vaginal cuff and reduce abdominal contamination to a minimum, thus insuring a safer postoperative period.

Postradiation Treatment of Carcinoma of the Cervix (3 Patients)

Routine.—Within forty-eight hours following removal of the radium, one Furacin vaginal suppository is inserted into the vagina twice daily following vinegar douches. This therapy is maintained for 2 to 3 weeks. Depending upon the patient's response, the suppositories are reduced to once daily when feasible.

Results.—There was a remarkable reduction in the amount of vaginal discharge which was practically odorless. The patient experienced a "soothing" sensation in the vagina in contrast to the usual rough, irritated feeling.

Although the number of cases in this group is much too small to draw any valid conclusions, the excellent results obtained warrant further continuation of this type of treatment.

Untoward Reactions

Only one of the ninety patients in this study complained of slight vaginal itching after 8 days of vaginal medication. This symptom ceased promptly when the medication was discontinued. This patient had been treated by electrocauterization for a cervical erosion. No other apparent allergic reactions were noted.

Summary

Furacin vaginal suppositories were used in 90 cases for the pre- and postoperative treatment of the vagina and cervix. They contribute to a smoother postoperative course in both vaginal and cervical surgery. When used postoperatively in cases requiring cauterization or conization of the cervix, as compared to other techniques, they reduced the healing time and markedly decreased the slough and malodorous discharge. These suppositories when used both pre- and postoperatively in total abdominal hysterectomies resulted in smoother and quicker healing. In the postradiation treatment for carcinoma of the cervix, Furacin vaginal suppositories inserted daily caused a marked decrease in slough and malodorous discharge.

In only one case among the 90 patients was any vaginal sensitivity to this dosage form of Furacin noted. The symptoms ceased promptly upon discontinuation of therapy.

Grateful acknowledgment is accorded to Dr. William Farrell, former resident, for his cooperation and assistance.

References

1. Marbach, H. A.: AM. J. OBST. & GYNEC. 55: 511, 1948.
2. Slater, Florence C.: AM. J. OBST. & GYNEC. 59: 1089, 1950.
3. Schottmüller, H.: München med. Wehnschr. 75: 1480, 1928.
4. Rakoff, A. E., Feo, L. G., and Goldstein, L.: AM. J. OBST. & GYNEC. 47: 467, 1944.
5. Dodd, M. C.: J. Pharmacol. & Exper. Therap. 86: 311, 1946.

134 HEMPSTEAD AVENUE.

TRANSVERSE PRESENTATION

Experience With Transverse Presentation at Baltimore City Hospitals and University Hospital Over a Period of Ten Years

LOUIS C. GAREIS, M.D., BALTIMORE, MD., AND MAJOR JOHN C. RITZENTHALER,
UNITED STATES ARMY, FT. MONMOUTH, N. J.

THE problem of the proper handling of the complication of transverse presentation in pregnancy and labor has become somewhat more complex in recent years, and there does not appear to be complete unanimity, even among teaching clinics. The following is a report of two fairly large clinics over a period of 10 years, Jan. 1, 1940, to Jan. 1, 1950. In it will be found figures and tables as to incidence, possible etiology, complications, results to mother and baby, etc., and a résumé of how the condition was treated. This is offered primarily for the purpose of comparison and with the hope that it will help in clarifying somewhat the entire problem.

Material

In the 10-year period there were treated 162 cases of transverse presentation or an incidence of one case in 322 deliveries. This is compared with the reports of other authors in Table I.

TABLE I. INCIDENCE OF TRANSVERSE PRESENTATION

De Lee	1 in 200
Torpin	1 in 1,090
Novey	1 in 250
Present report	1 in 322

In these two clinics we designate transverse presentation as a shoulder presentation and do not use the superior and inferior varieties as some clinics do. We found that there was no great preponderance in any particular presentation. The following is the incidence of the various types of transverse presentation in those that were actually diagnosed on admission.

TABLE II. INCIDENCE OF VARIOUS TYPES OF TRANSVERSE PRESENTATION

POSITION	NUMBER OF CASES	PERCENTAGE
Left acromiodorsum anterior	27	16.7
Left acromiodorsum posterior	29	17.9
Right acromiodorsum posterior	26	16.1
Right acromiodorsum anterior	26	16.1
Undesignated transverse	54	33.2
	162	100.0

It is to be noted that in 54 cases the transverse was undesignated; this is probably due to the fact that many transverse presentations are not recognized early in labor. X-ray was not used frequently as a diagnostic procedure, except in recent years, therefore, the exact presentation was not definitely known in a great number of cases. This is being corrected; transverse presentations are diagnosed much earlier and x-ray is used in a much greater number of cases of bizarre presentation.

TABLE III. SOME REASONS FOR TRANSVERSE PRESENTATION
MULTIPARITY

PARITY	NO. OF CASES	
0	22	
i	40	
ii	20	} 86.7
iii	17	
iv	17	
v	10	
vi	10	
vii	6	
viii	7	
ix	2	
x	5	
xi	5	
xii	1	
	162	
86.7 per cent para i or better; 49.4 per cent para iii or better		

Some of the more common reasons for transverse presentations were found in our review of 162 cases. Multiparity is frequently given as a reason because the relaxed uterus and the abdominal wall permit an unusual degree of mobility of the fetus. The following figures seem to bear this out. Table III shows that 86.7 per cent of the cases occurred in multigravidas, 86.7 per cent were para i or better, 49.4 per cent were para iii or better. There were 18 cases of twin pregnancies, the second twin being a transverse in all the cases. There was one case of triplets. Transverse presentation in the second twin in multiple pregnancy is much less serious because the cervix is fully dilated and the birth canal is prepared and the second fetal sac is usually unruptured. We had no fetal mortality in the second twin even though there was a prematurity rate of 34 per cent.

TABLE IV. SOME REASONS FOR TRANSVERSE PRESENTATION (CONTINUED)

COMPLICATIONS	NO. OF CASES	PERCENTAGE
Premature rupture of membranes	27	16.6
Bicornute uterus	3	1.9
Uterine fibroids	2	1.2
Contracted pelvis	16	9.9
Cephalopelvic disproportion	3	1.9
Lumbar scoliosis	1	0.6
Polydramnios	3	1.9
Low implantation of placenta and placenta previa	19	11.7

Premature rupture of the membranes apparently plays an important part in the etiology of transverse presentation and without this accident many pregnancies would continue on to term. With ruptured membranes apparently the fetus is fixed in position as the amniotic fluid escapes. Coupled with this is the frequency of prolapse of the cord or of fetal parts. Premature rupture

of membranes occurred in 16.6 per cent of the cases and since this is frequently an occurrence before the onset of premature labor it is to be noted that premature labor was present in 19.1 per cent; therefore, premature labor seldom occurs without premature rupture of membranes in our experience. Of those cases with premature rupture of membranes, in 55 per cent there was prolapse of a fetal part and in 51.6 per cent prolapse of the umbilical cord. As noted before, premature labor occurred in 31 cases as a natural sequence following premature rupture of the membranes and seldom occurred without this complication. Contracted pelvis is often mentioned as a contributing factor to transverse presentation, since the presenting part cannot engage in the inlet and in the process of labor a longitudinal presentation may convert to transverse presentation, or it may be a transverse presentation before the onset of labor because of the failure of the presenting part to negotiate or become engaged in the inlet. There were 16 cases of contracted pelvis and cephalopelvic disproportion, an incidence of 9.9 per cent. There were 3 cases of bicornute uterus, or an incidence of 1.9 per cent. There was probably more cases of uterine malformation, but they were not found, because the uterus prior to a few years ago was not routinely explored following transverse presentation. Indeed, experience seems to indicate that many cases of transverse presentation which are unexplained may be due to congenital deformities of the uterus. A form of lumbar scoliosis occurred in one case, and polyhydramnios in three cases. There was a high incidence of placenta previa or low implantation of the placenta. This is in keeping with recent reports, such as Stevenson's, which reports 92 per cent of placentas are implanted in either one or the other pole of the uterus. In this series 11.7 per cent of the cases had placenta previa or premature separation. We realize that there are many other reasons for transverse presentation, but these were some which seemed to be most frequently observed. In addition, there seemed to be a high percentage of cases in which the reasons for transverse presentation remained a mystery.

Complications of Transverse Presentation

Thus 29.0 per cent of the patients exhibited hemorrhagic symptoms.

As mentioned, of particular note is the high incidence of low implantation of placenta and placenta previa. This complication not only contributes to the presentation, but gives rise to hemorrhagic complications and we found that 29 per cent of our cases exhibited either antepartum, intrapartum, or postpartum hemorrhage.

TABLE V. HEMORRHAGIC COMPLICATIONS OF TRANSVERSE PRESENTATION

Antepartum hemorrhage	33	29%
Intrapartum hemorrhage	7	
Postpartum hemorrhage	7	

TABLE V.A. HEMORRHAGIC COMPLICATIONS OF TRANSVERSE PRESENTATION

Low implanted placenta	6
Placenta previa partialis	8
Placenta previa centralis	5
Premature separation of placenta	19
Ruptured uterus	5

The part which transverse presentation played in premature separation of the placenta is not definitely known; however, it is interesting to note that 19 cases exhibited some type of premature separation of the placenta. There

were five cases of rupture of the uterus and these, also, contributed to the hemorrhagic symptoms. Since so many cases were complicated by bleeding it is to be pointed out that a transverse presentation is an obstetrical emergency, and should be treated as such, and that procrastination does not seem to be advisable, except in an occasional selected case.

TABLE VI. INCIDENCE OF PROLAPSED FETAL PART IN TRANSVERSE PRESENTATION

FETAL PART	NO. OF CASES	PERCENTAGE
Cord only	14	8.6
Cord and arm	23	14.2
Arm only	35	21.6
Hand and foot	3	1.9
	75	46.3

Other complications which seem to be extremely important in the transverse presentation are prolapse of fetal parts. We found that 46.3 per cent of the total cases exhibited some type of prolapse of the cord or of a fetal part. In 22.8 per cent of the cases prolapse of the cord was noted. Since prolapse of the cord and fetal parts is so common a complication, it would seem as though this would be an additional factor which would stimulate the emergency treatment of such cases, for the sooner delivery is consummated, the less is the chance of this complication. Therefore, we feel in our clinics that the use of cesarean section and early delivery will, in many cases, prevent this complication from occurring, as well as the common hemorrhagic symptoms which we so frequently found.

TABLE VII. DURATION OF LABOR IN TRANSVERSE PRESENTATION

NO. OF CASES	DURATION OF LABOR LESS THAN 6 HOURS	PERCENTAGE	STILLBIRTHS	PER CENT OF FETAL MORTALITY
40		24.7	12	30.0
37	6 to 12 hours	22.8	18	48.6
41	13 to 24 hours	24.3	17	41.5
24	24 plus hours	14.8	15	62.5
Total 142				

In 20 cases the duration of labor was not determined; there were 7 stillbirths in this group.

The duration of labor was determinable in 142 cases. Fetal outcome according to labor duration was also noted with interest. Figures as presented in Table VII agree very closely with those of Epperson and Harris, thus it would seem, from study of our figures on duration of labor, that the longer labor is allowed to continue, the higher would be our fetal mortality rate. If it lasts over 24 hours the rate increases to 62 per cent. However, even though labor has not progressed for any great length of time, it is to be noted that fetal mortality is still exceptionally high. In 20 cases the duration of labor was not determined accurately, therefore we did not include them in our figures, even though there were 7 stillbirths in these 20 cases. At this point it seems fitting to mention that we had no figures on the diagnosis of the complication on admission. However, it seems to indicate that the earlier it is made the sooner appropriate treatment can be carried out. Epperson and Harris stress this point in that they found only 7 per cent fetal mortality in cases which were diagnosed early, having a 48 per cent cesarean section rate.

TABLE VIII. TREATMENT OF TRANSVERSE PRESENTATION

OPERATION	NO. OF CASES	STILLBIRTHS	UNCORRECTED
			PER CENT OF FETAL MORTALITY
External version	17	0 term 3 prem.	17.6
Internal podalic version and breech extraction	81	15 term 14 prem.	35.8
Cesarean section	32	3 term 5 prem.	25.0
Spontaneous evolution	6	6	100.0
Destructive operations	13	13	100.0
Fillet to foot	1	1	100.0
Braxton Hicks version	4	2 term 2 prem.	100.0
Spontaneous rupture of uterus	1	1	100.0
Undetermined	1	0	0.0

The various types of treatment, as seen in Table VIII with which these cases were handled at Baltimore City Hospitals and University Hospital, are listed. In those cases treated by external version it is to be noted that this procedure was carried out with the patient in labor; therefore, it was not possible to turn many of these babies externally, but, even so, external version seems to give us a lower fetal mortality rate than any of the other procedures. The use of external version prior to the onset of labor, or in the last four weeks of pregnancy, is to be encouraged. Attempts at external version, if gently done, are not harmful but the use of anesthesia is questionable. It is also our experience that probably Stevenson is correct in recommending placentograms on patients who are near term and exhibit transverse presentations persistently. Internal podalic version and breech extraction were carried out in 50 per cent of the cases with a 35.8 per cent fetal mortality. This operation was done in neglected cases usually and the procedure was done much more frequently in years past. Recently the use of cesarean section has become much more popular in our clinics. Nineteen per cent of the cases were treated by cesarean section, giving a fetal mortality rate of 25 per cent. Obviously spontaneous evolution is not to be relied on as the method of delivery. It occurs frequently in smaller babies in neglected cases and occasionally occurs in cases near term. In the six cases in which spontaneous evolution occurred there was 100 per cent fetal mortality. This would seem to indicate that spontaneous evolution does occur, but is very dangerous for the fetus. Destructive operations were carried out in 13 cases and obviously gave 100 per cent fetal mortality. A fillet was applied to the foot in one case of a small fetus with 100 per cent fetal mortality. Braxton Hicks version was used occasionally and of course gave a high fetal mortality. There were two spontaneous ruptures of the uterus which gave 100 per cent fetal mortality; the other three ruptures of the uterus reported were cases in which internal podalic version and breech extractions were carried out. A breakdown of the various procedures is given in the following table.

Thus it would seem from our experience that in any treatment of transverse presentation external version should be considered as a first procedure.

TABLE IX. EXTERNAL VERSION IN TRANSVERSE PRESENTATION

External version only	10
External version plus Willett clamp	2
External version plus abdominal binder	5
<i>Internal Podalic Version</i>	
81 cases, an incidence for the operation of 50%	

In the absence of rupture of the membranes, or prolapse of a fetal part, it may be successful. Should the membranes be ruptured it is doubtful if external version should be tried because of the danger of prolapse of the cord. If the fetal part is fixed in the pelvis with rupture of the membranes, external version is usually not possible. The use of external version without anesthesia prior to the onset of labor is carried out in our clinic routinely. Cesarean section is the next less lethal method of procedure. We had 25 per cent fetal mortality and no maternal deaths in this particular group. Stevenson reported a 34 per cent cesarean section rate with a fetal mortality rate of 13.4 per cent which is much better than we could report. Our experience with use of internal version and breech extraction has been that it is an extremely dangerous procedure because of the possibility of the rupture of the uterus. It can be used with more safety in the delivery of the second twin. It may be used in occasional cases in which we have the superior variety of transverse presentation with the lower extremities accessible at the inlet. It can be used occasionally in multiparas in whom the cervix is fully dilated and the lower extremities are easily accessible. We do not, as a rule, allow patients to continue in labor with the hope that an internal podalic version and breech extraction can be carried out when the cervix becomes fully dilated. It is our policy rather to do cesarean sections in these cases even though we have the prolapse of the presenting part and even though there may be some infection present. We feel that this can be controlled fairly satisfactorily today and if the fetus is alive we have a better chance for fetal survival, as well as a lesser chance of rupture of the uterus if the patient is delivered abdominally. Should the patient be frankly infected we feel that a cesarean hysterectomy may be in order. We have not been very successful in doing extraperitoneal cesarean sections in cases of transverse presentation.

TABLE X. TYPES OF CESAREAN SECTION IN TRANSVERSE PRESENTATION

Laparotrachelotomy	15	} 19.8%
Laparotrachelotomy plus supravaginal hysterectomy	2	
Classical cesarean section only	10	
Classical cesarean section and sterilization	3	
Classical cesarean section and supravaginal hysterectomy	2	
	32	

Laparotrachelotomies were done in 15 of the cases and these were those cases which occurred within the past few years. The longitudinal incision has been found more satisfactory in that the fetus is more easily accessible for delivery after the uterine incision is made, than the transverse, in which the incision is somewhat limited in extent. If the operator finds difficulty in delivering the infant in transverse presentation through a longitudinal incision, this type of incision can be extended to allow more room for delivery. The two classical cesarean sections and supravaginal hysterectomies were done in cases in which the patients were infected and were not done in recent years. In review, then, our present policy is to treat these patients more radically. We are using cesarean section more frequently and are relying very little on internal podalic version and breech extraction. In this way we feel that we avoid a high fetal mortality, we have less danger of rupture of the uterus, and we feel that, since infection plays a smaller role in maternal mortality, we can be more radical in our treatment.

A review of the types of destructive operations which were carried out in neglected cases of transverse presentation showed an incidence of 8.3 per cent, or 13 cases. Various operations are listed in Table XI. Decapitation is

TABLE XI. DESTRUCTIVE OPERATIONS IN TRANSVERSE PRESENTATION

Fillet to right arm, disarticulation of right arm, craniotomy and internal podalic version and breech extraction	2
Fillet to left arm, decapitation	1
Decapitation only	5
Right shoulder resection, thoracic evisceration	1
Right shoulder resection and decapitation	3
Amputation of arm followed by internal podalic version and breech extraction	1
	13

the operation of choice, especially in the case of a prolapsed arm. After decapitation traction on the arm will deliver the body and the head can be delivered by bimanual manipulation. Destructive operations are done only if the fetus has died and the cervix is fully or almost fully dilated. Decapitation was carried out in nine of the 13 cases of destructive operations. The uterus was explored in 22, or 28 per cent, of the cases which we reviewed; however, it is to be noted that the routine exploration of the uterus is only of recent origin. X-ray was also used as a diagnostic aid in only a relatively few cases. Recently we have been using x-ray more liberally.

TABLE XII. FETAL MORTALITY IN TRANSVERSE PRESENTATION

		NO.		
Over 1,000 grams	Full-term living children	77	47.4	60.4%
	Premature living children	21	13.0	
	Full-term stillborn infants	29	17.9	37.7%
	Premature stillborn infants	32	19.8	
	Abortions, late	3	1.9	1.9%
Uncorrected fetal mortality rate 37.7%				

We found that we had a 37.7 per cent uncorrected fetal mortality, in both full-term and premature babies (that is, babies over 1,000 grams). We included in these cases only babies who were stillborn or who died shortly after delivery. There is little doubt that neonatal deaths in these cases are exceptionally high and if we had added fetal deaths occurring in the first 24 hours we would have a much higher fetal mortality rate. Certainly we feel that if many of these cases had been treated more radically we would have a much better fetal salvage. Maternal morbidity occurred in 44 cases, or 27.2 per cent; this is a temperature over 100.4° F. for two days or more. Maternal mortality of this series was the two cases, or 1.9 per cent. A review of the two maternal deaths follows:

CASE 1.—J. W., aged 25 years, Negro, unregistered, para iv-0-0-iv, was admitted on July 13, 1940, because of vaginal bleeding at term. Previous obstetrical history: Her first delivery was terminated by midforceps; the second by cesarean section because of placenta previa. On July 8 the patient began having vaginal bleeding. On July 9 labor began and membranes ruptured July 10 at 3 P.M. The patient suddenly became pale and showed signs of shock. A sterile pelvic examination revealed the cord to be prolapsed, not pulsating, and the position to be left acromiodorsum posterior. Following the sterile pelvic examination the patient began to bleed profusely and went into profound shock. Blood transfusions were started and the patient was delivered immediately by internal podalic version and breech extraction July 10, 1940. The uterus, cervix, and vagina were explored and found to be intact. The patient remained in shock and developed a severe postpartum infection. In spite of heroic measures, her condition grew gradually worse. Respiration ceased on July 18, 1940. Cause of death: Bronchopneumonia and puerperal sepsis?

CASE 2.—A 44-year-old, white, para xii-0-0-viii, was admitted for treatment of hypertension on Dec. 1, 1946. Several previous pregnancies were complicated by hypertension. On Dec. 7, 1946, labor began. After four hours no progress had been made and an x-ray revealed transverse presentation (head against the spinal column and breech against the anterior abdominal wall—Resident's note: "An A.P. positional variety of transverse lie"). After 14 hours and no progress, a classical cesarean section was done. Following delivery the patient developed a severe postpartum infection which terminated in death from peritonitis.

There were five cases of rupture of the uterus, two spontaneous ruptures and three following internal podalic version and breech extraction; in all of these cases hysterectomy was done.

Summary and Conclusions

1. Incidence and experience with transverse presentation at Baltimore City Hospitals and University Hospital for a period of 10 years have been presented.

2. There were 162 cases, or one in each 322 cases.

3. Factors which contributed to the occurrence of transverse presentation are presented: multiparity, premature rupture of the membranes, premature labor, bicornuate uterus, contracted pelvis, lumbar scoliosis, polydramnios, low implantation of the placenta, and placenta previa.

4. Hemorrhagic complications were found to be very common: 29 per cent of the cases had hemorrhagic complications; 11.7 per cent had placenta previa or low implantation of the placenta. This seems to verify Stevenson's contention that the position of the placenta greatly influences the presentation of the fetus.

5. Prolapse of the fetal part or cord is common: 46.3 per cent.

6. Fetal mortality increases in direct proportion to the duration of labor.

7. Cesarean section is the choice of treatment when the baby is living, unless the patient is first seen with the cervix fully dilated or nearly so, or internal version can be done easily. Cesarean section gives greater fetal salvage and is safer for the mother. It is to be pointed out that various papers on rupture of the uterus give internal podalic version and breech extraction a very high place in the causes of such complications. Douglass and Morrison in their report on rupture of the uterus indicate that version and breech extactions are the second greatest causes of rupture of the uterus, previous cesarean section being first. Two cases of neglected transverse presentation were mentioned by Douglass and Morrison in their paper; there was 100 per cent maternal mortality, with rupture of the uterus in both cases.

8. In doing a cesarean section, the use of the longitudinal incision is recommended since the transverse one limits the uterine incision in length and direction. A longitudinal incision can be extended if the fetus is impacted at the inlet, or if the uterus is tightly applied to the fetus. A transverse incision is difficult to extend. Extraperitoneal section is difficult to do with this type of complication and we have had very little success with it in our clinic.

9. External version should always be tried, even though the patient is in active labor, especially if she is seen early in labor. It should always be at-

tempted in the last trimester, when the diagnosis of a transverse presentation has been made. We subscribe wholeheartedly to Stevenson's contention that x-ray placentography should be done in the last trimester of pregnancy when a transverse presentation persists, to locate the placenta.

10. The destructive operation of choice is decapitation if the fetus is found dead.

11. The uterus should be explored in all cases of vaginal delivery of a transverse presentation to rule out rupture of this organ.

12. Experience shows that diagnosis is made early in only 50 per cent of the cases; x-ray should be liberally used in all questionable presentations. Placentography is recommended when diagnosis is made in the last ten days of pregnancy.

13. A fetal mortality rate, uncorrected, of 37 per cent can be expected. We feel that more liberal use of cesarean section would improve fetal salvage.

14. Most common maternal complications are hemorrhagic conditions and puerperal infection. Since puerperal infection now has taken a secondary place, hemorrhagic complications can be defeated by more radical treatment, that is, cesarean section. The most immediate danger of transverse presentation is rupture of the uterus.

We wish to emphasize that the above statements are merely our experiences with transverse presentation at the University Hospital and The Baltimore City Hospitals within the past 10 years. We do not urge cesarean section for treatment of all cases of transverse presentation, but merely have found from our experience that the use of a more radical approach will probably give us better fetal salvage and probably will decrease maternal mortality and morbidity.

References

- Stevenson, C. S.: *AM. J. OBST. & GYNEC.* 58: 432, 1949.
Morrison, J. Huff, and Douglass, Louis H.: *AM. J. OBST. & GYNEC.* 50: 330, 1945.
Eastman, Nicholson J.: *Williams Obstetrics*, ed. 10, New York, 1950, Appleton-Century-Crofts Company, Inc.
Epperson, J. W., and Harris, Bruce: *AM. J. OBST. & GYNEC.* 59: 1105, 1950.
Eastman, N. J.: *AM. J. OBST. & GYNEC.* 24: 40, 1932.
Torpin, R.: *AM. J. OBST. & GYNEC.* 39: 92, 1940.
Novy, M. A., and Snyder, M. M.: *AM. J. OBST. & GYNEC.* 41: 53, 1941.

MYOMECTOMY

Surgical Technique and Results in a Series of 1,150 Cases

ARTHUR M. DAVIDS, M.D., NEW YORK, N. Y.

(From the Gynecological Service of Mount Sinai Hospital)

THE trend toward radical pelvic surgery has increased in recent years. The total extirpation of the uterus has to a great extent replaced the previous simple supravaginal hysterectomy. The extensive Wertheim operation with pelvic node dissection has again been advocated in certain centers for irradiation of early carcinoma of the cervix. This same attitude, however, has not been evident in facing the problem of conservation of the genitals. Hysterectomies are being performed in increasing numbers on patients who would like to retain their menstrual and reproductive functions. It is indeed illogical to observe the physician who on the one hand will spend endless time and effort initiating and maintaining the menses with endocrine therapy in some patients while on the other hand he will deprive others of their menstrual and reproductive functions merely because of the presence of single or multiple fibromyomas. An analysis of a series of hysterectomies by Miller¹ in 1946 revealed that in 33.1 per cent of the cases there was either no disease or else disease contraindicating hysterectomy. In this group of cases 44 per cent of the women were below the age of 40 years. With this in mind it would seem opportune to present our attitudes and experiences on the Mount Sinai Hospital Gynecological Service with respect to simple and multiple myomectomy. A series of 1,150 operations during the past 30 years will be reviewed and the pertinent clinical observations discussed.

The history of the operation of myomectomy extends back to 1840 when Anussat in France performed the first operation of its kind for a pedunculated fibroid. In 1898 the first report of radical multiple myomectomy was presented by W. Alexander² of Liverpool who removed 25 fibromyomas from a single uterus. This operation, however, has never been received with the enthusiasm it deserves. The advocates of the procedure such as Victor Bonney³ in England, Kelly,⁴ Noble,⁵ the Mayos,⁶ and Rubin⁷ in this country have repeatedly reported their excellent results but myomectomy still has not been widely practiced. This attitude is probably based upon earlier experiences before the routine use of transfusions, chemotherapy, antibiotics, and the modern techniques of anesthesia and surgery.

Material

From Jan. 1, 1921, to Dec. 31, 1950, 1,150 myomectomies were performed. The clinical data accumulated over the 30-year period have been analyzed and presented in detail.

The age incidence of fibroids in this series is presented in Table I. It is natural that 82.8 per cent of the myomectomies should be performed between the ages of 25 and 40 years during the most active reproductive life. There were, however, 7.2 per cent of the cases in the age group of 18 to 25 years. Five of these cases occurred before the age of 20 and in fact the largest single fibroid tumor (5 pounds, 6 ounces) was removed from an 18-year-old girl. This case will be presented later in more detail. The incidence of myomectomies falls from the age of 40 years and was performed in 10 per cent of our series between the ages of 40 and 73 years. On patients over 50 years of age 24 myomectomies were performed almost exclusively by the vaginal route. These cases are included in this series inasmuch as another 19 vaginal myomectomies were performed in the younger age group and an evaluation of this procedure is important.

The marital status and parity of the patients were as follows. There were 841, or 73.2 per cent, married patients and 309, or 26.8 per cent, single patients. Of the 841 married patients 432 conceived and had a total of 742 pregnancies. Only 439, or 59 per cent, of these pregnancies produced viable infants. There were 303 miscarriages, an incidence of 41 per cent of the total pregnancies. Repeated abortion due to the presence of fibroids is demonstrated by the incidence of 69 patients with a history of 2 to 5 miscarriages.

TABLE I

AGE (YEARS)	NUMBER OF CASES
15-20	5
21-25	78
26-30	227
31-35	491
36-40	235
41-45	76
46-50	16
51-60	14
61-70	9
71-80	1

The largest group of patients, 467, presented themselves for operation because of infertility or repeated miscarriages. Many of these patients had associated symptoms due to the fibroids but their prime motivation in submitting to surgery was for the purpose of enhancing conception and ultimately delivering a viable infant. The other patients had chief complaints of menorrhagia and menometrorrhagia in 363 cases, the presence of an increasing abdominal mass in 210 cases, dysmenorrhea in 138 cases, and abdominal pain or pressure symptoms in 195 cases. In all these patients excepting the postmenopausal patients, the desire either for conception or retention of menstrual function was foremost in the mind of the patient and myomectomy was the procedure of choice.

Technique

The success or failure of the attempted myomectomy hinges on many factors. No patient should be unequivocally promised that a myomectomy will be performed. Despite the best of intentions and careful preoperative study unexpected pathology found at operation may make myomectomy impossible or inadvisable. Such conditions, however, present themselves in the minority of cases and the number of successful myomectomies will be in proportion to the enthusiasm of the surgeon for the procedure. The size, number, and location of the fibroids should be no contraindication to the procedure.

The preoperative preparation is important. Many of these patients enter the hospital with a very low hemoglobin having had long periods of irregular

and profuse bleeding. The blood loss must be corrected by repeated transfusions and operation should be deferred until the patient's blood count is relatively normal. Blood should always be available for transfusion during and after the operation. The routine use of hysterosalpingography preliminary to operation is a great aid in planning surgery. If the uterine cavity is normal on x-ray visualization there is no necessity to perform a preliminary curettage or to explore the uterine cavity at the time of myomectomy. However, the discovery of a small submucous fibroid or uterine polyps forewarns the surgeon of the necessity of entering the uterine cavity. The failure to remove such polyps or submucous fibroids will defeat the purpose of the operation as excessive menstrual flow will continue despite the removal of the submucous and intramural fibroids which are present.

Success at the outset may be best insured by the proper exposure of the uterus through an adequate abdominal incision. The Pfannenstiel incision should be used only in the presence of a fibroid uterus which is no larger than an 8 to 12 weeks' gestation. Limited exposure may force the surgeon to abandon a myomectomy which could be accomplished easily through a larger and less limiting incision. In the presence of large fibroids a paramedian or midline incision which may be lengthened by a hockey-stick extension is the incision of choice. The uterus is exposed and if possible delivered through the abdominal incision. The entire pelvic situation is now appraised, the condition of the adnexa, the number, size, and location of the fibroids, the most advantageous location for the major incision or incisions into the uterine wall, and the possibility of insuring maximum hemostasis either by uterine tourniquet or Bonney clamp. Where feasible the use of a uterine tourniquet will insure almost a bloodless field during a major portion of the operative procedure. Rubin introduced the use of the rubber tourniquet in the following fashion at this institution in 1938.

A twelve-inch length of Dakin's tubing is threaded through a large Gallie needle. The needle is passed through the free space in the right broad ligament about 1 to 1½ inches outside the lateral margin of the cervix and a short distance above the supravaginal level of the cervix. It is passed anterior to the cervix and then through the left broad ligament in a similar location. The tubing is then stretched taut and crossed behind the cervix just above the insertion of the uterosacral ligaments. It is then clamped with an Ochsner clamp at the point of crossing of the tubing. This procedure compresses the ascending uterine vessels and produces almost complete hemostasis. It has been found unnecessary to clamp the broad ligament and tubes since minimal bleeding is encountered from the branches of the ovarian vessels. The tourniquet can be applied for from 10 to 15 minutes and then loosened for a minute or two. It is then again tightened and clamped. This has been done repeatedly through a two-hour procedure with no ill effects on the healing process in the myometrium. Hemostasis obtained in this fashion gives the surgeon ample opportunity to work in an almost bloodless field for the enucleation of large and small tumors and for a careful reconstruction of the uterus.

The planning of the uterine incisions is of the utmost importance. The number of incisions is kept to a minimum and if possible limited to the anterior superior surface of the uterus. If possible the incisions should be made in the midline or over the tumors in such fashion as not to compromise the uterotubal junctions. Posterior wall incisions should be either transverse below the line of insertion of the Fallopian tubes or as near the midline as possible. The largest fibroid is located for the site of the primary incision and then a linear incision is made boldly through the myometrium and capsule of the fibroid partially bisecting the tumor. Both halves of the fibroid are grasped with tenaculi and the fibroid removed by intracapsular dissection with the handle of the scalpel or by sweeping the finger boldly around the fibroid. At a few

places the capsule may be densely adherent and this may be freed by sharp dissection. Once the largest tumor is removed an attempt is made to remove the smaller ones by tunneling into the myometrium through the enucleated fibroid bed. These fibroids are partially bisected in similar fashion and in most instances can be enucleated by twisting the tenaculi which grasp the two halves. If a submucous fibroid is present the incision is carried downward directly into the uterine cavity and the submucous fibroid removed. Submucous fibroids originating from the posterior uterine wall can also be enucleated through an anterior wall incision and the bed sutured with ease. In fact, in the presence of a large cervical fibroid involving the cervical canal or uterine cavity the anterior approach through the cavity is the one of choice. When all the fibroids that can be enucleated through the one incision are removed the resulting cavity or cavities are obliterated with two or three layers of continuous catgut sutures. The use of the continuous suture saves a great deal of time, produces good hemostasis, and has not in any case hampered healing of the myometrium. In reconstructing the uterine wall little or none of the redundant musculature should be trimmed away. The loose flaps may be imbricated to advantage so that the uterine wound is under no tension and a final layer of serosal sutures may be passed without difficulty. If all the fibroids have not been removed through the one incision they are now attacked in the same fashion as in the primary incision. Posterior wall fibroids are attacked in a similar fashion.

Large intraligamentous or large cervical fibroids are no contraindication to myomectomy. In the presence of a large cervical fibroid the bladder flap of large peritoneum is incised and the bladder pushed down from its attachment to the lower uterine segment and fibroid. The fibroid is boldly incised and partially hemisected, as previously described, and removed. If the cervical canal is opened widely a rubber tubing may be passed from the uterine cavity through the external os and the cervical canal reconstructed over the rubber tubing to avoid the obliteration of the canal. In an unusual case Counseller⁸ successfully anastomosed a cervix and uterine fundus following the removal of a cervical fibroid which required transection of the elongated cervix.

Intraligamentous fibroids of large size may occur. They are best handled by opening the broad ligament which is stretched over them. An area free of vessels is found on the surface of the fibroid and the capsule incised. An intracapsular removal avoids excessive bleeding and in most cases does not necessitate ligation of the uterine vessels. However, if this is necessary, it can be done without hesitation and without detriment to healing of the uterus. An interesting case to illustrate this will be cited.

At the termination of the myomectomy, postoperative complications can be greatly reduced if the uterine wounds are carefully peritonized. The wounds on the anterior and superior surfaces of the uterus can be effectively extra-peritonized by freeing the vesicouterine flap of peritoneum and resuturing the flap over the anterior surface of the uterus. The posterior incisions may be covered by either suturing the appendices epiploicae of the sigmoid or actually suturing the sigmoid serosa to the posterior uterine wall. An omental graft also may be utilized effectively to cover an extensive incision of the posterior uterine wall.

At the termination of a radical myomectomy the reconstructed uterus may be the size of a 3 to 4 months' gestation. This is due to the marked hypertrophy of the myometrium about the numerous fibroids. The conservation of all this myometrium insures a reconstruction of the walls without undue tension. The hypertrophied myometrium involutes in a similar fashion to that of a pregnant uterus but at a much slower rate. The uterine cavity may return to normal size

and shape within 8 to 10 days but the uterus itself may not involute completely for 10 to 12 weeks.

The removal of fibroids by the vaginal route is feasible in certain cases. An aborting submucous fibroid if small may be removed by simple avulsion. One may encounter a large aborting submucous fibroid in conjunction with intramural and subserous fibroids. If such a situation occurs the aborting fibroid should be removed by splitting its capsule and then avulsion. Bleeding can be controlled by actual ligation of the pedicle or by packing the uterine cavity. The abdominal removal of the other uterine fibroids should be deferred to some later date. Not infrequently a patient suffering from severe menometrorrhagia may have a uterus normal in size or only slightly enlarged. Hystero-graphy or curettage may reveal a solitary submucous fibroid. Such solitary submucous tumors can be removed by performing a vaginal hysterotomy and enucleating the fibroid. The uterine cavity is packed to avoid bleeding.

TABLE II

NUMBER OF FIBROIDS	NUMBER OF CASES
1	457
2	186
3	144
4	99
5	69
6	44
7	23
8	31
9	17
10	16
11	10
12	9
13	3
14	6
15	7
16	3
17	3
18	2
19	3
20	2
21	4
22	1
23	1
24	1
25	1
28	1
30	1
32	1
33	1
35	1
43	1
60	1
80	1

The number of fibroids removed at operation is listed in Table II. A simple myomectomy was performed in 457, or 39.7 per cent, of the total number of cases. Multiple myomectomy was performed in 693, or 60.3 per cent. The largest number of fibroids removed from a single uterus was 80. It would be of interest at this point to present the case histories of a number of the author's patients to demonstrate certain important clinical features.

CASE 1.—R. G., aged 30 years, was admitted to the hospital because of the presence of a large abdominal mass and severe menorrhagia. She had been married for 10 years but had never conceived. She had not practiced contraception during this period. The

general physical examination was negative except for the presence of a large irregular abdominal mass. Pelvic examination revealed a normal vulva and vagina. The cervix was clean. The uterus was enlarged by multiple fibroids to the size of an 8 months' gestation. No adnexal masses could be delineated. A preoperative hysteroqram (Fig. 1)



Fig. 1.—Case R. G. Preoperative hysteroqram revealing a markedly enlarged uterine cavity with multiple filling defects in its upper third.

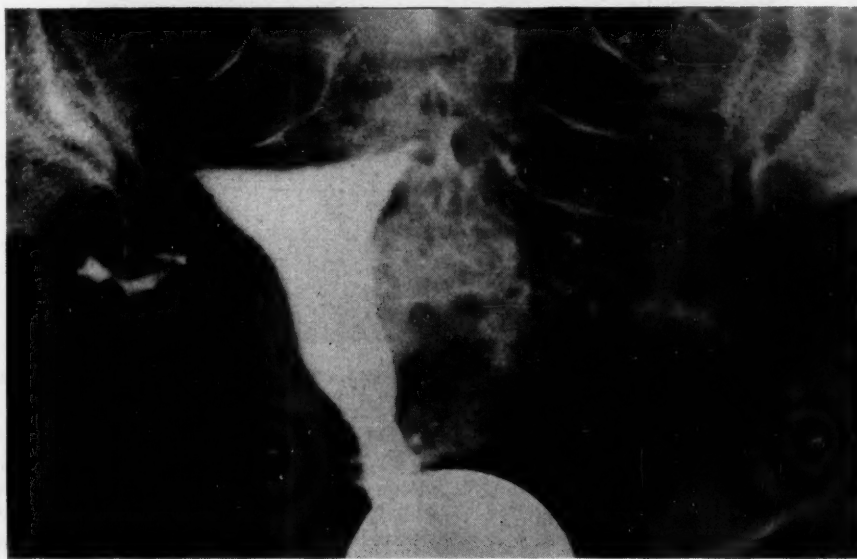


Fig. 2.—Case R. G. Hysteroqram three months postoperatively revealing a normal uterine cavity with normal patent Fallopian tubes.

revealed a markedly enlarged uterine cavity with the presence of submucous fibroids. The patient's hemoglobin was 60 per cent and she was given two transfusions of 500 c.c. of blood before operation. At operation the adnexa were found to be normal. The uterus

was enlarged by intramural, intraligamentous, and submucous fibroids. Because of the presence of large intraligamentous fibroids, a uterine tourniquet could not be utilized. The bladder was freed from its attachment to a large subvesicle fibroid and then a multiple myomectomy was performed. Sixty fibroids weighing $6\frac{1}{4}$ pounds were removed. The uterine cavity was entered and three submucous fibroids found. The uterus was reconstructed without the excision of any of the redundant musculature. At the termination of the operation the uterus was the size of a $3\frac{1}{2}$ to 4 months' gestation. The anterior uterine wound was completely peritonized by reattaching the bladder flap of peritoneum high upon the fundus of the uterus. The posterior wall incisions were covered by suturing the sigmoid epiploicae to the posterior uterine wall. The patient was transfused during the operation and immediately postoperatively. She received a total of 2,000 c.c. of blood. The duration of operation was 1 hour and 45 minutes. The patient's postoperative reaction was excellent despite a febrile course for 8 days. During the first three days her temperature ranged between 102° and 103.4° F. but she showed little systemic effect otherwise. There was minimal distention and she was ambulatory after the second postoperative day. Pelvic examination on the sixteenth postoperative day revealed the uterus to be the size of a $3\frac{1}{2}$ months' gestation. She was discharged to be followed in the clinic and 3 months later the uterus was normal in size. Hysterography at this time revealed a normal uterine cavity and normal tubal patency (Fig. 2).



Fig. 3.—Case A. R. Preoperative hystero-gram revealing a large filling defect with distortion of the uterine cavity due to a submucous fibroid.

CASE 2.—A. R., aged 25 years, single, gravida 0, entered the hospital because of severe menometrorrhagia and weakness. She had had a previous hospital admission six months before at which time her hemoglobin was 32 per cent. She was given seven transfusions at that time and curetted. The uterus was symmetrical and the size of a 6 to 8 weeks' gestation. An irregularity of the endometrial cavity was felt during the curettage. The pathological report was hyperplastic endometrium. The patient continued to have menorrhagia following the curettage and she was readmitted to the hospital. The uterus had enlarged and at this time was the size of a 3 months' gestation. Hystero-graph revealed a large submucous fibroid (Fig. 3). The hemoglobin was 59 per cent and the patient was given 1,500 c.c. of blood preoperatively. A myomectomy was performed and a single large

submucous fibroid was removed. The uterine cavity was entered during the procedure. The patient's postoperative course was uneventful. She was febrile for five days, the highest temperature reaching 101.6° F. A hysteroqram was performed on the eleventh postoperative day and revealed a normal-sized uterine cavity (Fig. 4). At discharge on the thirteenth day the uterus was the size of an 8 weeks' gestation. She was seen again 4 weeks postoperatively and on pelvic examination the uterus was found to be normal in size, freely movable, and nontender.

CASE 3.—M. M., aged 18 years, married, gravida 0, entered the hospital because of the presence of a large abdominal mass, dyspareunia, and frequency of urination. Her menses were scant and irregular. General physical examination was negative except for the abdominal and pelvic findings. The vulva was normal. On insertion of a finger into the vagina, a mass was encountered just within the vagina and filling the entire pelvis. The cervix could not be felt or visualized. The pelvic mass was hard and fixed and extended into the abdomen to a level 3 fingerbreadths below the xyphoid. A flat plate of the abdomen revealed a large soft tissue mass occupying the pelvis and abdomen.

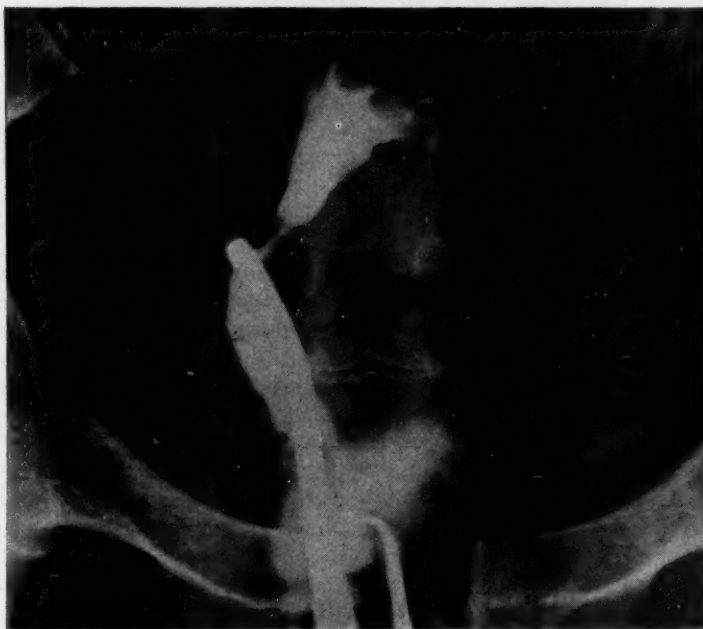


Fig. 4.—Case A. R. Hysteroqram performed on the eleventh postoperative day showing a normal sized and shaped uterine cavity.

At operation the abdomen was entered through a long paramedian incision and a single large fibroid was found occupying the pelvis and abdomen. It was intraligamentous in origin and the right tube and ovary surmounted the fibroid tumor. On the left side of the tumor at about the level of the umbilicus a small flattened uterine body was identified and a normal left tube and ovary were present. The peritoneum covering the tumor was incised and the bladder freed from its anterior aspects. A number of large vessels entering the fibroid on its right lateral aspect were ligated and the tumor then elevated from its bed. As this was done, the right ureter, the vena cava, and aorta were visualized to the level of the right kidney. The vessels of the right infundibulopelvic ligament had been ligated as they coursed over the tumor since the right ovary now had no lateral attachment. There was no identifiable capsule to the tumor mass so that the flattened uterine body was freed from it by sharp dissection. The right tube which was greatly elongated was clamped and cut. With the removal of the tumor a hemisectioned

elongated uterus remained. There were no uterine vessels present on the right side of the remaining uterine body. The uterus was reconstructed by approximating the musculature with two layers of sutures and at the termination of the procedure the uterus had the appearance of a congenital single-horned structure. The retroperitoneal space was easily peritonized by the redundant peritoneum previously freed from the tumor. The patient had an uneventful postoperative course. She was febrile for four days, the temperature being 103° F. on the first day and never subsequently rising above 101°. At the time of discharge on the fourteenth day the uterus was found to be just slightly enlarged. The cervix was visualized and found to be normal. The patient refused to use contraceptives and 3 months following the operation she conceived. The pregnancy was uneventful and a cesarean section was performed in the thirty-eighth week. One and one-half years later the patient again became pregnant and a cesarean section was again performed in the thirty-eighth week.

There is still hesitancy on the part of some surgeons to open the endometrial cavity during myomectomy and many surgeons automatically favor hysterectomy in the presence of a large submucous fibroid. In this series the endometrial cavity was entered in 153 cases with no increase in the postoperative morbidity. There has been no report of a single ruptured uterus in subsequent pregnancies carried to term and delivered normally or by cesarean section. Bonney states that in the majority of cases of myomectomy it is desirable to open and explore the cavity of the uterus, for otherwise it is quite easy to overlook a small submucous fibroid or polyp. In so doing, the surgeon may leave behind the chief cause of the menorrhagia for which the operation may have been done. The routine exploration of the uterine cavity is unnecessary however if hystero-graphy is performed preoperatively.

Myomectomy during pregnancy was performed in 35 cases. The operations were done before viability of the fetus because of severe pain due either to degeneration of a fibroid or to the enlargement of a fibroid producing severe pressure symptoms. In this group the pregnancies ranged from 6 to 18 weeks in duration. Twenty-three, or 65.7 per cent, of the cases carried to term. Four pregnancies were interrupted at the time of operation because the uterine cavity and amniotic sac were entered inadvertently during the procedure. Eight patients aborted spontaneously during convalescence in the hospital. The largest number of fibroids removed during pregnancy was 15. In this case the patient was 8 weeks pregnant, had an uneventful convalescence and carried to term.

The length of time required to perform a myomectomy varies greatly and depends on many factors. Speed in itself, however, is unimportant. When a great many fibroids are present the surgeon must necessarily work rapidly and systematically unless he wants to expose the patient to an unduly long anesthesia. The cases of very short duration were cases of simple vaginal myomectomies. In 810 cases, or 70.4 per cent, the duration was one hour or less. In the remaining 340 cases the duration was from 1 hour and 15 minutes to 2 hours and 40 minutes. It is of interest to note that duration of operation and length of anesthesia had no direct bearing on the morbidity or mortality. In the cases where death occurred, all were performed in an hour or less except one. In this latter case, the longest in duration, 2 hours and 40 minutes, a multiple procedure of vaginal plastic, multiple myomectomy, and appendectomy were performed. The problem of multiple procedures associated with myomectomy will be discussed later.

The anesthesia of choice will vary in one institution or another depending upon the training of the anesthetists. The anesthesia of choice at Mount Sinai Hospital is inhalation anesthesia and 1,090 patients, or 94.7 per cent, were anesthetized in this fashion.

Myomectomy alone was performed in 860 cases, or 74.7 per cent. The presence of tubal or ovarian disease in 156 cases necessitated salpingo-oophorectomy in 53 cases, ovarian resection in 58 cases, and tubal plastic operations in 40 cases. Conservative surgery for benign ovarian pathology is certainly indicated if one undertakes to perform an extensive myomectomy for reproductive purposes. Ovarian resection should be performed whenever possible. Pregnancy has resulted in many cases in which both myomectomy and ovarian resection were performed. Despite the poor results of tubal plastic procedures in general, a plastic operation was performed in 40 cases. The simple knowledge of the possibility of conception, no matter how slim, is of great psychological import to some patients. Vaginal myomectomy was performed in 43 cases with good results. In the elderly patients the simple vaginal operation obviated the much more serious risk of laparotomy and eradicated the cause of bleeding.

The association of appendectomy and myomectomy is a question open to some disagreement. It was done in only 70 cases in this series. Appendectomy undoubtedly can be performed with relative safety in conjunction with a simple myomectomy. However, it would seem ill advised to complicate an extensive operative procedure for multiple fibroids by doing an appendectomy at the same time. In 5 of the 10 deaths that occurred an appendectomy had also been performed. Despite the fact that these fatalities occurred before the use of antibiotics we still feel strongly that the combined procedure is not a good one. Other procedures such as vaginal plastic repairs in conjunction with myomectomies are no longer done. The 17 such cases in this series were all performed in the early group of cases.

The pathological report was uncomplicated fibromyomas in 802, or 69.7 per cent, of the cases. There were 5 cases in which definite malignant changes were found in fibroids that had been removed. In 3 cases the findings were spindle-cell sarcoma and in 2 myosarcoma. In 7 other cases the pathological diagnosis of cellular fibroid was made. All 12 cases were treated conservatively without x-ray therapy or further surgery. The patients were followed carefully and in no case was a recurrence encountered. Three patients in this group became pregnant with no untoward result. In 114 cases the pathological diagnosis was fibromyomas with necrosis or degeneration. The presence of degeneration in the fibroids did not seem to affect the morbidity of the patients. The process is almost always an aseptic one and does not introduce a hazard to the myomectomy.

The morbidity and mortality associated with myomectomy have changed greatly during the past 30 years. There were 10 deaths in the entire series of 1,150 cases, or a mortality of 0.86 per cent. This figure, however, must be clarified. During the period between 1921 and 1935, 225 myomectomies were performed with 9 deaths or a mortality of 4 per cent. During the period between 1936 and 1950, 925 myomectomies were performed with 1 death, or a mortality of 0.1 per cent. This is an extremely low mortality rate. The distinct change in the two eras is also similarly seen in other fields of surgery. With the use of chemotherapy, antibiotics, liberal use of blood transfusions, and other modern supportive therapy the morbidity and mortality have steadily fallen. During the period between 1921 and 1935 the cause of death of 6 of the patients at autopsy was found to be generalized peritonitis and ileus, in 2, bilateral bronchopneumonia, and in 1 ileus and pulmonary embolism. The 1 death occurring between 1936 and 1950 was due to a massive pulmonary embolism. The 8 deaths due to infection during the first 15-year period could in great part now be forestalled by modern therapeutic measures. Bonney in reporting a series of 987 cases accumulated over a period of 37 years had a mortality rate of 1.3 per cent. In a recent article from New York Hospital, Finn and Miller⁹ report a series of 432 myomectomies during the period between 1932 and 1947

without a single mortality. The morbidity of myomectomy has similarly been reduced during the past 15 years. Generalized or pelvic peritonitis, postoperative pneumonia, kidney infections, septic thrombophlebitis, and wound complications are no longer a frequent hazard of myomectomy. The morbidity, by the standard of the American College of Surgeons, 100.4° F. on any two days excluding the day of operation, reveals that 1,003 cases ran a morbid course. Seven hundred twenty-nine, or 63.1 per cent, of the patients were afebrile at the end of 4 days and 953, or 82.8 per cent, were afebrile at the end of 10 days. The convalescence following myomectomy is not unduly long; 221 patients were discharged from the hospital by the tenth day and 972, or 84.5 per cent, by the fifteenth day.

The frequency of pregnancy following myomectomy cannot be accurately stated in this series. The follow-up after one year is too inadequate to give a true figure. However, on questioning individual gynecologists on the service we find that the frequency of pregnancy in their own cases varies from 30 to 50 per cent. Bonney states that on the basis of his cases 38 per cent of the patients myomectomized during the childbearing age may be expected to conceive. In the New York Hospital series, 212 of 432 patients were adequately followed and the pregnancy rate of the patients who were desirous of pregnancy was 48.5 per cent. The pregnancy rate for the entire series regardless of desire was 25 per cent. The method of delivery following myomectomy should generally be governed by the ordinary obstetrical indications that arise. Previous myomectomy in itself is no indication for cesarean section. In the New York Hospital series 83 per cent of the patients were delivered vaginally without untoward results. In only 5 of the 11 patients delivered by cesarean section was previous myomectomy the indication. Bonney states that of the children born after myomectomy, some 75 per cent are born naturally or could be so born. In his group the proportion of cesarean sections was high not because natural labor was impossible but because many of the women were pregnant for the first time at a relatively advanced age, so that the survival of the child was of more than usual consequence.

The recurrence of fibroids following myomectomy depends upon many factors. The age at which myomectomy is performed is one of the most important. When fibroids occur at an early age a special tendency to the formation of these tumors must be inferred. It is in these young women that the conservation of the uterus is most pressing. The recurrences will be in direct proportion to the care with which the surgeon removes the smallest seedlings as well as the larger fibroids. In most cases recurrences are due to small fibroids or seedlings present at the time of operation and not removed. The subsequent growth of fibroids, however, may not necessarily require hysterectomy. In this series only 5 per cent of the patients returned for secondary surgery. Bonney reports that 3 per cent of his patients required a hysterectomy at a later date. In the New York Hospital series 23 per cent of the patients had a reappearance of fibroids but only 12 per cent were symptomatic and required hysterectomy.

Comment and Summary

The psychological impact of the loss of the uterus may be so profound as to affect the entire life pattern. Marriage and propagation are the ultimate social and biologic goals. The woman deprived of her ability to conceive is definitely handicapped in her attainment of marriage. In our series, 309, or 26.8 per cent, of the patients were single and it would seem that the preservation of the uterus in such cases would be almost mandatory. The barren marriage is fraught with emotional disturbance and may lead to great unhappiness. Infertility and repeated miscarriages are frequently due to the presence of

fibromyomas. Forty per cent of the women in our series presented themselves for relief from such problems. These patients are greatly relieved when they can be assured that pregnancy is not only possible but likely following myomectomy. The mere fact that the possibility of future conception exists is often sufficient to salvage a marriage and relieve the patient's anxieties. It was with this in mind that in 40 cases tubal plastic procedures were performed in conjunction with myomectomy. Many of the women between the ages of 40 and 45 were newly married and despite the lowered incidence of pregnancy in the fifth decade they elected to have a myomectomy performed rather than submit to hysterectomy.

The castration effect of the loss of the uterus may have serious repercussions in the normal sex life of many patients. All information to the contrary, many women still believe that removal of the uterus and loss of menses is associated with a reduction of libido and sexual desirability. This situation may produce or seriously aggravate neurotic tendencies. In cases where patients are suffering from obvious neuroses or are under psychiatric treatment the surgeon should be reluctant to consider hysterectomy unless absolutely necessary.

There is no doubt that where the reproductive functions have been satisfied and there is no psychological contraindication hysterectomy is the operation of choice. The election of hysterectomy cannot be made however on the supposition that morbidity and mortality are less than with myomectomy. The morbidity and mortality figures of our series during the past 15 years (0.1 per cent) and the absence of a single mortality in the New York Hospital series of 432 cases compares favorably with any series of hysterectomies reported during a similar period.

The recurrence of fibromyomas is not a serious contraindication to myomectomy. In the unmarried woman or the married woman who has not successfully completed her family this should not be a consideration. Any woman who has been able to bear a child following myomectomy will gladly risk the possibility of a second surgical procedure. The recurrence rate of 2.3 per cent in Bonney's large series and a 5 per cent recurrence rate in our own series indicates that this is not a great hazard. The recurrence of fibroids does not necessarily mean that surgery is a necessity. Many of these patients may be carried either to their menopause without further treatment or others if symptomatic may be treated with either intrauterine radium or x-ray therapy. It is only in the younger age groups where ovarian function should be retained that repeated surgery may be indicated.

The surgical techniques and the method of obtaining hemostasis have been described in detail and have eliminated the hazards of hemorrhage and shock. The liberal use of blood, chemotherapy, and antibiotics has reduced the morbidity and mortality to the point where multiple myomectomy is no longer a formidable procedure.

The careful preoperative study of patients by Papanicolaou smears, cervical biopsy, hysterosalpingography, and, if necessary, dilatation and curettage will eliminate the possibility of performing a myomectomy in the presence of a cervical or endometrial carcinoma. No cases of carcinoma were encountered in this series. If at operation a very fleshy tumor showing degenerative changes is found a frozen section should be performed. Sarcomatous degeneration in a fibroid was found in five cases and in seven cases a report of cellular fibroid was made. Where the diagnosis of sarcoma is made the surgeon must weigh carefully the factors which shall determine his choice of myomectomy or hysterectomy. The size and total removability of the involved tumor are of primary importance. The patient's age, parity, and her determination to bear children must next be considered. In our 5 cases of sarcoma the fibroids involved with

malignant changes were completely removed and the uteri retained. There were no recurrences in any instance despite the fact that 3 of these patients became pregnant.

The number and location of fibroids are no contraindication to myomectomy. If proper hemostasis is obtained it is possible to remove a great many fibroids. The largest number of fibroids removed from a single uterus in our series was 80. Bonney, however, has removed as many as 225 fibroids from a single uterus and still reconstructed a normally functioning organ. Submucous fibromas should no longer in themselves be an indication for hysterectomy. There was no increase in morbidity or mortality in the 153 instances in which the endometrial cavity was entered to remove one or more submucous fibroids. The accurate suturing of the fibroid bed prevents any undue postoperative bleeding. In none of the 153 cases was postoperative bleeding a problem.

The preservation of the uterus by myomectomy has resulted in frequent pregnancies. The results in different series will vary depending upon such factors as the ages of the patients, their marital status and desire for children, the associated adnexal pathology, and the length and accuracy of the follow-up studies. On the basis of our own and other studies, pregnancy following myomectomy can be predicted in approximately 30 to 50 per cent of the patients who make a sustained effort to conceive. Such results should be sufficient reward for any surgical procedure and for the surgeon's painstaking efforts. The incidence of uterine fibroids is great and myomectomy is the only method by which the menstrual and reproductive functions can be preserved.

References

1. Miller, N. F.: *AM. J. OBST. & GYNEC.* 51: 804, 1946.
2. Alexander, W.: *Brit. Gynaec. J.* 14: 47, 1898.
3. Bonney, V.: *J. Obst. & Gynaec. Brit. Emp.* 44: 1, 1937.
4. Kelly, Howard A.: *Am. Med. Ass. Press*, 1907, pp. 1-2.
5. Noble, Charles P.: *Myomectomy*, New York, 1906, A. R. Elliott Publishing Co.
6. Mayo, William J.: *Surg., Gynec. & Obst.* 34: 548, 1922.
7. Rubin, I. C.: *AM. J. OBST. & GYNEC.* 44: 196, 1942.
8. Counseller, Virgil S.: *J. A. M. A.* 109: 1687, 1937.
9. Finn, W. F., and Miller, P. F.: *AM. J. OBST. & GYNEC.* 60: 109, 1950.

123 EAST 83RD STREET

MESODERMAL MIXED TUMOR OF THE CORPUS UTERI*†

THOMAS W. McELIN, M.D., M.S., AND HARWELL DAVIS, JR., M.D.,
CHICAGO, ILL.

(From the Department of Obstetrics and Gynecology and the Department of Pathology,
Northwestern University Medical School and The Evanston Hospital)

IT IS our purpose to present two previously unreported instances of mesodermal mixed tumor of the uterine corpus. It is of interest that this rare, highly malignant, monodermal uterine lesion was encountered twice within a period of one week in the last year at the Evanston Hospital. Furthermore, it is noteworthy that these are the only instances of this uterine tumor that have ever been observed at this hospital.

Lebowich and Ehrlich,¹ who have presented the most complete review of this subject that has appeared in the last decade, state that because of the rarity of these tumors, their unusually variegated structure, and the complex queries regarding histogenesis which they inevitably provoke, the recording of each new case is a medical obligation.

It is not our purpose to review the literature at great length nor to engage in extended controversy concerning differential diagnosis or histogenesis. However, a brief examination of the published data will serve as a convenient point of departure for our case reports.

Where in a classification of malignant tumors of the uterine corpus is a mesodermal mixed tumor to be properly placed? This neoplasm may properly be regarded as a sarcoma. The two principal varieties of sarcoma of the uterus are the myometrial and endometrial variants. It has been stated that myometrial sarcomas represent approximately 75 per cent of the total in large series of cases and, of these, about two-thirds are "secondary" in that they spring from pre-existing fibromyomas and one-third are "primary" in that they arise directly from the myometrium. We are not concerned at the moment with the myometrial variety. About 25 per cent of uterine sarcomas are endometrial and it is with this subheading of corporeal malignancy that we are concerned. Of these, 80 per cent are pure fibromyxosarcomas of the endometrial stroma and 20 per cent are mesodermal mixed tumors.²

We, therefore, are concerned with an unusual variant of endometrial sarcoma which we recognize to be a group that is statistically less frequent than the more common myometrial variety and we know that the entire group of uterine sarcomas constitute only about 4½ per cent³ of the malignant tumors of the uterus.

How, then, does a given tumor qualify to enter this statistical sanctum sanctorum? It is obvious from even cursory examination of the literature that the requisites for admission depend upon the authority cited and are at wide variance. Murphy and DuShane,⁴ however, have logically pointed out that the varying figures of incidence and the varying rigidity of

*Presented before the Chicago Gynecological Society, May 18, 1951.

†Grateful acknowledgment is made to Dr. William Cummings, Evanston, Ill., for permission to include Case 2.

diagnostic criteria in no way detract from the interest in or importance of this group of tumors. It would, however, seem proper to consider primarily the most rigid of the admission requirements. These are the criteria of L  wen⁵ which have been emphasized so forcefully by Lebowich and Ehrlich¹ and Ehrlich⁶ in the past decade. These authors have repeatedly stressed that embryonal striated muscle cells in association with one or more heterologous elements must be present before the diagnosis of mesodermal mixed tumor may be substantiated. Ehrlich felt that fifteen true examples of this tumor had been reported by 1941. Morehead and Bowman⁷ presented an intermediate opinion in 1945. They felt it unwise to exclude all but those containing striated myoblasts since mesodermal mixed tumors are a pathologic entity and a group, clinically. Still less rigid than this position is that of Glass and Goldsmith,⁸ who stated that ninety-four tumors in this group had been identified in the corpus and in the cervix of the uterus.

Meikle,⁹ in 1936, prepared a thesis on the subject of mesodermal mixed tumors and defended the utilization of criteria less rigid than L  wen's. He stated that many tumors which truly deserve inclusion within this group contain only early embryonic muscle fibers in which the transverse striations are not yet well developed. Shapiro¹⁰ was also quoted to the effect that a positive diagnosis can be made without definitely seeing striated cells. Shapiro regarded as suggestive the presence of large cells with vesicular and often multiple nuclei, centrally placed within a deeply eosinophilic, finely granular, and often vacuolated cytoplasm. Glynn and Blair-Bell¹¹ also observed this type of cell.

Other types of tissue which have been observed include myxomatous connective tissue, cartilage, bone, fat, lymphatic tissue, smooth muscle, and squamous-cell elements.¹ The extreme vascularity of the tissues has been commented upon in the literature. Benign-appearing glandular structures which are similar to endometrial gland formation have been observed within the substance of these tumors. An incredibly complete epithelial covering of these tumors has been commented upon many times in the literature.

The various theories as to histogenesis of these bizarre tumors have been adequately reviewed by others and no recent information would seem to lend added weight to any of these. The existing theories may be summarized in brief by title: Wolffian duct remnant theory, M  llerian cell rest theory, teratomatous origin, and the occurrence of dedifferentiation with neoplasia.

There is nothing in the clinical history or physical examination of these patients that is suggestive of the ultimate diagnosis. Precise classification of the lesion and definitive entry of a diagnosis on the patient's record awaits the pathologist's evaluation of the excised tissue. Radical abdominal surgery and postoperative irradiation constitute the treatment of choice despite the known radioresistance, the almost inevitable reoccurrence, and the foreboding prognosis.

Case Reports

CASE 1.—A 53-year-old married woman, gravida ii, para ii, was admitted to the Evanston Hospital on July 1, 1950. The patient complained of intermittent vaginal bleeding and of fatigue since September, 1949. She had experienced a roentgen-induced menopause at age 42, eleven years prior to admission. Precise information concerning the radiotherapy administered elsewhere was unobtainable but it seems that the patient received treatments of approximately 400 r to each of four pelvic portals. She had experienced no genital bleeding following this procedure until the onset of the present episode.

The first episode of vaginal bleeding in September of 1949 was of two days' duration and, thereafter, vaginal bleeding occurred in a somewhat cyclic fashion at intervals of about three weeks. Contact bleeding or dyspareunia had not occurred.

General physical examination was within normal limits. The patient had refused pelvic examination in the office of her gynecologist and similarly refused pelvic examination at the time of hospital admission. She had, however, consented to the obtaining of a specimen of vaginal secretion for the performance of cytologic study. A report was returned to the effect that conclusively malignant cells were observed. Accordingly, with full application of this psychological lever, the patient consented to the performance of a dilatation and curettage for definitive diagnosis.

A definite intrauterine mass was identified with the curette on the posterior surface of the uterine cavity. A considerable amount of fleshlike material was obtained. The operator specifically commented that, although the curettings were suggestive of malignancy, the material was highly atypical and did not resemble the usual endometrial adenocarcinoma.

The pathologist ultimately reported that the tissue received was composed of a mixture of malignant elements and suggested the diagnosis of mesodermal mixed tumor.

Accordingly, on July 5, 1950, total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed. The specimen consisted of the uterus (6 by 4 by 3 cm.), tubes and ovaries, and these structures were normal in gross appearance. When the uterus was opened, a gritty, irregular, and moderately soft mass of tissue—unattached to the endometrium—occupied the endometrial cavity. A similar mass of tissue was noted attached near the mid-point of the fundus. The total tumor formed a mass approximately 10 c.c. in volume.

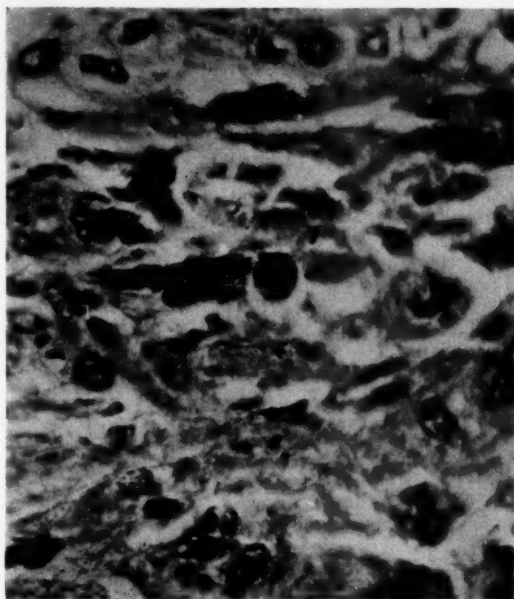


Fig. 1.

Fig. 1.—Giant and "strap" cells, thought to be primitive muscle cells.

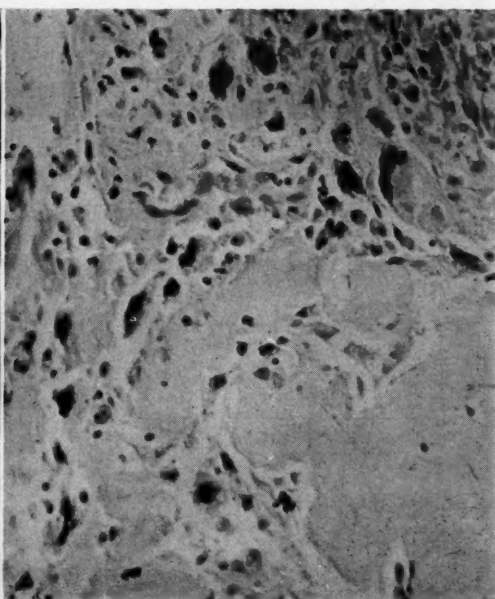


Fig. 2.

Fig. 2.—Giant cells associated with osteoid tissue.

Microscopically, the greatest part of the tumor consisted of mesenchymal tissue in varying stages of differentiation. In one area, straplike cells, having fibrillar, eosinophilic cytoplasm were admixed with polymorphous, multinucleated giant cells. The nuclei here were hyperchromatic, irregular in size and shape (Fig. 1), occasionally having a "bearded" or fuzzy appearance. These cells were considered to be myoblasts. Transverse striations were demonstrated in a few cells in one such area. These latter were considered to be a more adult form of primitive muscle than the nonstriated cells seen in the same general location. Mitotic figures were frequent. In other areas, early and calcifying osteoid were

observed (Fig. 2). In another location, moderately adult cartilage was seen with a primitive perichondrium composed of spindle-shaped cells surrounding it (Fig. 3). Large areas of solid flat cells with moderate-sized nuclei which, at times, seemed to form small glandular

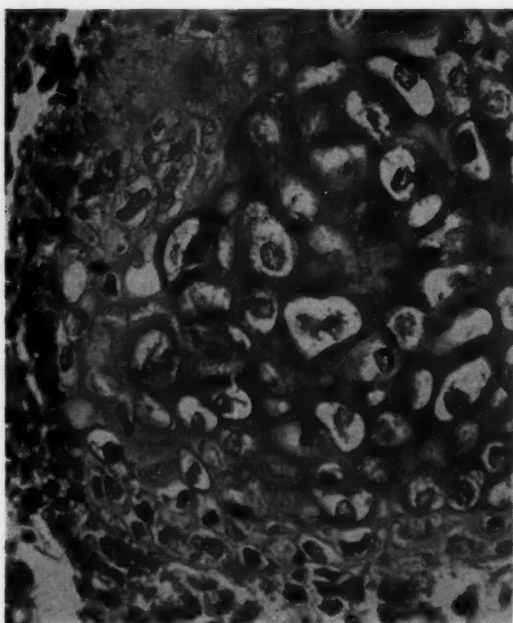
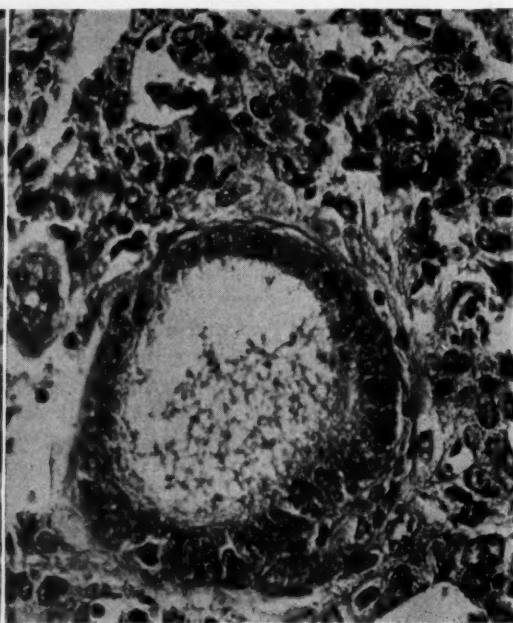


Fig. 3.



• Fig. 4.

Fig. 3.—Cartilage.

Fig. 4.—Gland of adult construction surrounded by undifferentiated mesenchyme.

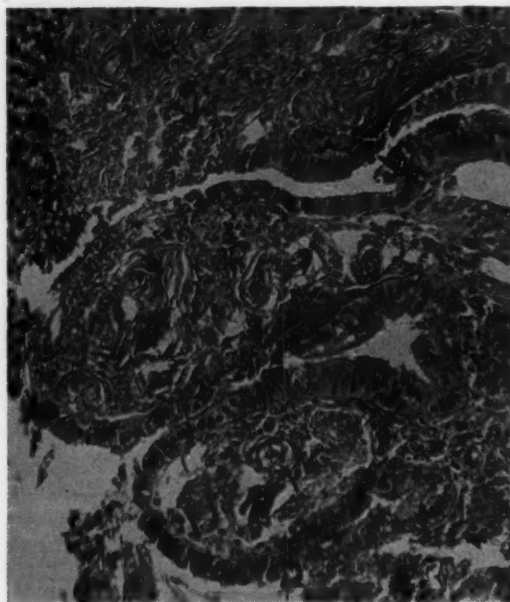


Fig. 5.

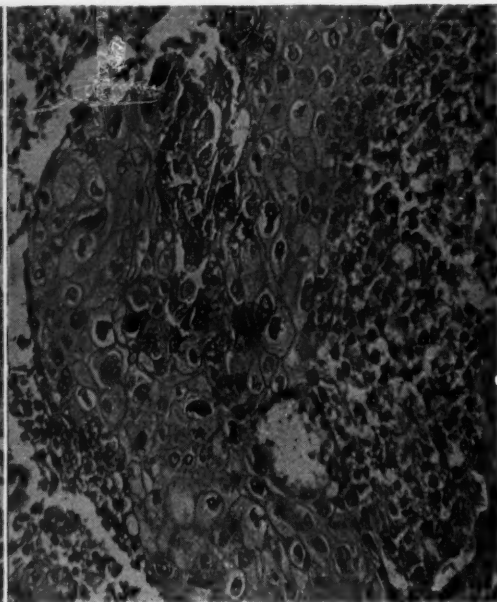


Fig. 6.

Fig. 5.—Peripheral border of tumor. Note adult construction of lining epithelial cells.

Fig. 6.—Area of squamous cells within tumor.

structures were seen (Fig. 4). Minimal invasion was to be seen beyond the peripheral epithelial border made up of relatively normal-appearing endometrial cells (Fig. 5). One area of squamous epithelium was present (Fig. 6).

Thus, cartilage, osteoid, a sort of poorly differentiated epithelium attempting to form rudimentary glands, squamous epithelium, as well as myoblasts, were present and were mixed with generous quantities of primitive mesenchyme. In addition, cross striations were unequivocally demonstrated in some primitive muscle cells.

To date the patient has received 2,000 r to the mid-pelvis on each side. This has been administered in three separate courses over a seven-month period. Fifteen months have now elapsed since surgery and there is no evidence of recurrence thus far.

CASE 2.—A 58-year-old married woman, gravida iv, para iii, entered Evanston Hospital on July 10, 1950. Her complaint was of a postmenopausal discharge of three and one-half weeks' duration. The discharge at first was white but, shortly prior to administration, had turned dark brown in color. A few days after the onset of the brown discharge she had experienced a cramping pain in the lower abdomen.

The last menstrual period had occurred twenty years prior to admission. She had been told at that time that she had a "fibrous uterus" and was given roentgen therapy for this condition. A "sterilization dose" of x-ray was said to have been administered. Tanning of the skin resulted from this therapy and the menses ceased. Her mother had died at age 75 of cancer of the uterus.

Physical examination revealed a well-developed and slightly obese woman. A blowing, precordial systolic murmur and infrequent extrasystoles were heard. The abdomen was described as protuberant, soft, and nontender. Vaginal examination revealed the uterus to be freely movable and distinctly enlarged. There were no palpable adnexal masses and there was no pelvic tenderness.

Laboratory data prior to surgery revealed a hemoglobin determination of 13 Gm. per cent, an erythrocyte count of 4,540,000, a normal leukocyte count and normal differential blood count. Serologic examination of the blood was negative. Urinalysis gave a normal result. Roentgenogram of the thorax was negative.

Total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed on July 11, 1950, under Pentothal Sodium and spinal anesthesia. The preoperative diagnosis was probable carcinoma of the uterine fundus. The uterus was found to be about twice normal size and several small fibromyomas were observed. The adnexa seemed quite normal.

Examination of the operative specimen showed the uterus to be 12 by 9 by 6 cm. in size. The entire uterine cavity was occupied by a soft, yellow, hemorrhagic, pedunculated mass measuring 8 cm. in greatest diameter. On section, the tissue was hemorrhagic and cystic, particularly at the periphery. The mass was attached to the uterus near the orifice of the left Fallopian tube. The cystic, congested endometrium measured 1 cm. in greatest thickness and contained two submucous myomas, one of which was totally calcified.

Microscopic examination of the tumor showed undifferentiated mesenchymal tissue. There were areas of spindle-shaped cells with eosinophilic cytoplasm and vesicular nuclei which seemed to be smooth-muscle precursors. Transverse striations were not demonstrated. Areas of giant cells, adult and primitive cartilage were seen. Near the base of the tumor were a few glands. Some of these were apparently of entirely adult structure while others were less well-differentiated. Many mitotic figures were present. Scattered throughout the tumor were rather large areas of necrosis and hemorrhage.

The postoperative course was completely uneventful. The patient has now received two series of deep x-ray treatments. Approximately 1,300 r have been delivered to the mid-pelvis within a period of four months. She is to receive another course of deep x-ray therapy. The patient is free of recurrence and metastasis at the present time and fifteen months have elapsed since surgery.

Summary and Conclusions

We have encountered two additional examples of mesodermal mixed tumor of the corpus uteri. We are well aware that only our first case meets the most rigid of the requirements for entrance into this select group of uterine neoplasms. Our second case did not give evidence of the cross striations in early muscle tissue as requested by L  wen.

We do not believe that the fifteen-month period of survival without evidence of metastasis in our cases is significant. It would be impossible to offer anything but a gloomy prognosis. We have deliberately avoided a discussion of the possible tumorigenic effect of x-ray in these cases. Such a discussion has not been considered pertinent.

It would seem, therefore, that our attitude toward management of this problem should be one of therapeutic totalism. Although we had an unusual opportunity in our first case to utilize every therapeutic opportunity, inasmuch as we had a preoperative diagnosis and no gross evidence of extrauterine extension, we perhaps did not so avail ourselves. Although a statistically significant series of such favorable cases would probably never appear during any reasonable period of time, it would be interesting to speculate on the possibility of improving the survival statistics with more radical management. Given an accurate preoperative diagnosis and no evidence of extrauterine involvement, one might well advise the performance of a total abdominal hysterectomy, bilateral salpingo-oophorectomy, and total pelvic lymph gland dissection followed by intensive postoperative x-ray to the pelvis and carefully screened radium to the vaginal vault and vaginal walls. We were, of course, somewhat limited in our x-ray therapy because both of these patients had had radiation treatment to the pelvis previously.

In all medical and surgical problems, when the future of a given patient is in dire jeopardy, it seems reasonable that every conceivable therapeutic procedure should be utilized unless the concomitant hazards are excessive.

References

1. Lebowich, R. J., and Ehrlich, H. E.: *Surgery* 10: 410, 1941.
2. DeVoe, R. W., Dockerty, M. B., and Pratt, J. H.: Personal communication.
3. Novak, E.: *Gynecological and Obstetrical Pathology*, Philadelphia, 1947, W. B. Saunders Company.
4. Murphy, G. H., and DuShane, J. W.: *AM. J. OBST. & GYNEC.* 55: 527, 1948.
5. L  wen, A.: Quoted by Lebowich, R. J., and Ehrlich, H. E.¹
6. Ehrlich, H. E.: *AM. J. OBST. & GYNEC.* 43: 1021, 1942.
7. Morehead, R. P., and Bowman, M. C.: *Am. J. Path.* 21: 53, 1945.
8. Glass, M., and Goldsmith, J. W., Jr.: *AM. J. OBST. & GYNEC.* 41: 309, 1941.
9. Meikle, G. J.: *J. Obst. & Gynaec. Brit. Emp.* 43: 821, 1936.
10. Shapiro, P. F.: *AM. J. OBST. & GYNEC.* 21: 83, 1931.
11. Glynn, E., and Blair-Bell, W.: Quoted by Meikle, G. J.⁹
12. Huffman, J. W.: *AM. J. OBST. & GYNEC.* 56: 23, 1948.
13. Wagner, E.: Quoted by Meikle, G. J.⁹
14. Weber, O.: Quoted by Meikle, G. J.⁹
15. Kehrner, E.: Quoted by Meikle, G. J.⁹
16. Pfannenstiel, J.: Quoted by Meikle, G. J.⁹
17. McFarland, J.: *Surg., Gynec. & Obst.* 61: 42, 1935.

Discussion

DR. RONALD R. GREENE.—I believe that everyone will accept the fact that the first tumor is an authentic mixed mesodermal tumor. Some will quibble or will refuse to accept the second tumor because cross striations were not found in the rhabdomyosarcomatous elements. In this I think they are illogical and wrong. All observers agree that the cells of these tissues resemble embryonic muscle cells or myoblasts. These cells develop from primitive mesenchymal cells. Early in differentiation myofibrils develop in the cytoplasm. Cross striations later develop in and from the myofibrils. The point is this: In very poorly differentiated or very embryonic rhabdomyosarcomatous tissue one would not expect to find cross striations since the individual cells are not mature enough or well-differentiated enough to have these structures.

I therefore believe that this second tumor should not be excluded merely because cross striations are not present. Incidentally, myofibrils are clearly discernible in some of the cells of this tumor.

On one point I do not see eye to eye with Dr. McElin and that is the probable value of extensive and repeated postoperative radiation. In general, tumors with sarcomatous elements metastasize via the blood stream. If these tumors have metastasized via the blood stream prior to operation, radiation therapy of the pelvis and lower abdominal regions do no more than make the patient miserable. I think I would be more in favor of letting the patient live her allotted span of time without this added discomfort.

DR. A. H. KLAWANS.—A couple of years back, in a Tumor Clinic, the pathologist and radiologist were discussing a case they were showing. They said that they were now seeing carcinomas of the skin occurring in patients who had benign tumors treated by radiation therapy or carbon dioxide snow therapy twenty or twenty-five years ago. I am asking whether radiation therapy of these two patients has been at all responsible for changing the character of the tumor to a malignant picture.

DR. HERBERT E. SCHMITZ.—I hesitate to make any remarks relative to the carcinogenic effect of irradiation. This carcinogenesis generally is admitted. I have not the slightest idea how many hundreds of thousands of people have been treated by all forms of irradiation in the past twenty-five years for benign and malignant conditions, but the incidence of carcinoma occurring in the skin in well-controlled therapy is negligible. We have all seen cases that have been overirradiated develop carcinoma in the skin. In patients with recurrence where it has been decided that surgical treatment would be of no benefit and, because of bleeding or pain the patient demands some further treatment, irradiation has been repeated—a so-called palliation irradiation which would have much destructive effect if the patient lives long enough, yet we must accept it as justifiable and prepare for secondary effects in those cases in which we succeed in arresting the disease.

There is absolutely no statistical proof up to the present time that there is any relationship between tumors of this type or adenocarcinoma of the endometrium and previous radiation therapy. Certainly the rarity of the tumor being discussed tonight is adequate proof in my mind that irradiation cannot be responsible for its cause.

DR. McELIN (Closing).—I am delighted to hear that Dr. Greene feels that the second—the less legitimate of our cases—should be accepted as a true case of mesodermal mixed tumor and should not be stigmatized by the absence of transverse striations. It seems to me that all through the literature there is too much emphasis on this particular point. There have been only two cases in this group of tumors that had had a four-year survival and it seems to me that the matter of whether these striations were or were not present is not too crucial.

Regarding Dr. Greene's comment as to ideal therapy, and his disagreement with my approach, I confess that I outlined my totalistic therapy to see what discussion would be provoked. The idea of this approach occurred to me because of two cases of mesodermal mixed tumors I have seen (cases not included in this paper), wherein the patients had

metastases to the vagina after total abdominal hysterectomy had been performed. These local recurrences were treated with radium and palliation was obtained. I had thought that the implantation type of metastases might be prevented by more thorough vaginal irradiation.

Dr. Greene mentioned that x-ray therapy seemed inappropriate to him in view of the gloomy prognosis that must be assigned to this tumor and that it might be more reasonable to spare the patient the known discomforts of strenuous radiotherapy.

This objection seems invalid to me for two reasons. First, I do not believe that we are ever justified in withholding any legitimate method of therapy. Second, if we reason from a histopathologic point of view, we note the amazing similarity of a mesodermal mixed tumor to the embryonal adenomyosarcoma of the kidney, or Wilm's tumor. The accepted method of management of this latter tumor is massive radiotherapy regardless of the initial stage of advancement. By analogous reasoning, radiotherapy for the tumor under discussion seems logical.

A question was asked regarding the methods of metastasis of this tumor. Lymphatic extension, blood stream extension, and implantation have all been mentioned in the literature.

I will not attempt to discuss the carcinogenic properties of x-ray as commented upon by Dr. Schmitz. In the literature that I have reviewed, I know of no other cases in which the patient had had x-ray treatment prior to the development of a mesodermal mixed tumor.

PROGESTERONE METABOLISM; I. PREGNANEDIOL EXCRETION IN THE MENSTRUAL CYCLE

RICHARD H. FISCHER, M.D., STANLEY P. MCCOLGAN, M.S., AND
ALBERT L. CHANEY, PH.D., WASHINGTON, D. C.

(From the Research Foundation, Doctors Hospital)

THE determination of urinary pregnanediol as an estimation of progesterone production has received considerable attention. Two primary methods of procedure with minor modifications have been used in such studies. The method of Venning¹ is dependent upon a determination of the glucuronide of the complex rather than pregnanediol. The method of Astwood and Jones² utilizes the measurement of pregnanediol following the hydrolysis of the complex. Stimulated by the work of Smith and Smith,³ many investigators^{4, 5, 6, 7} using the basic Astwood-Jones technique have failed to confirm the data obtained with the method of Venning. Recent investigations by Smith^{8, 9} have revealed that overestimations may occur with the method of Venning.

As the authors have had available a new and accurate method for determining the free pregnanediol, it was felt that perhaps new data pertaining to corpus luteum activity during the menstrual cycle could be elucidated. Apparently normal young women were studied for the majority of one complete cycle in an attempt to ascertain what constituted normal progesterone activity when measured by this method and to serve as a foundation for further studies in the metabolism of progesterone as determined by pregnanediol in the urine.

Materials

Women technicians and nurses of the Doctors Hospital and the Hunter Laboratories volunteered to serve as participants in this investigation. Facts pertaining to their menstrual and obstetrical histories were obtained at the completion of each study. Individual 24-hour urine specimens were collected without preservative and the pregnanediol determined within the succeeding 24-hour period.

Method

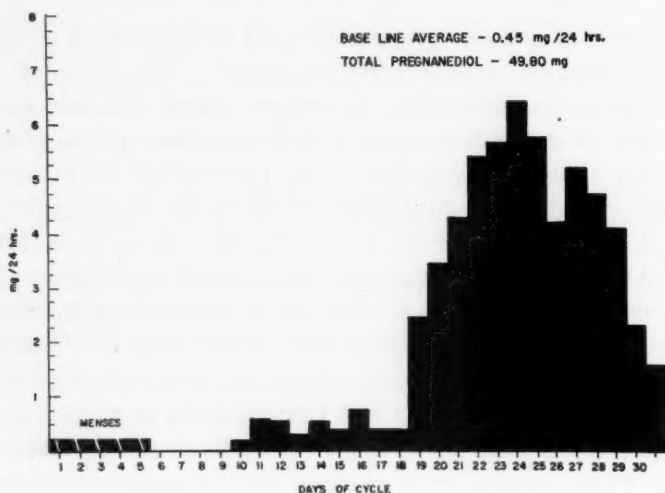
The procedure for the determination of free pregnanediol as devised by Chaney and McKee¹⁰ was utilized in this study. Details of the procedure and a critical evaluation of its accuracy are presented elsewhere.

Results

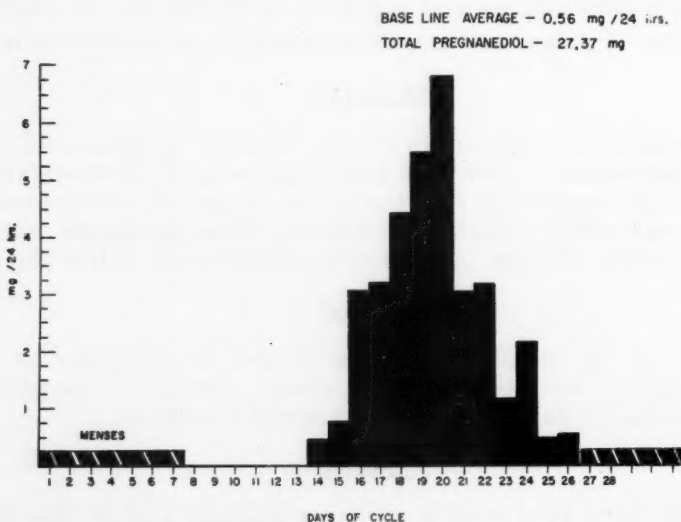
The authors have been unable, utilizing sulfuric acid in this colorimetric method, to obtain a zero reading. There seems to be sufficient invisible material in the final flask to interfere with transmission as compared to the sulfuric acid blank. Although it is possible that this may represent extremely small quantities of crystalline pregnanediol, no such claims are made. In computing the total pregnanediol excreted per cycle, the daily averages during the pre-ovulatory phase have been subtracted from the total values in the postovulatory period.

CASE 1.—A 23-year-old married white woman, para 0, gravida 0, reported the onset of menses at the age of 12 years and the rapid assumption of a regular cyclic pattern. The

usual interval between periods was 25 days with 5 days of menstrual flow. Clots occurred with each period, small in size and moderate in number. She had mild lower abdominal cramps on the first day of menstruation. There was no indication of a premenstrual prodrome. Pregnanediol first appeared in the urine on the nineteenth day and reached a maximum level of 6.5 mg. on the twenty-fourth day of the cycle. Pregnanediol was still present in the urine on the day of onset of menstruation. The total quantity of pregnanediol excreted was 49.8 mg.



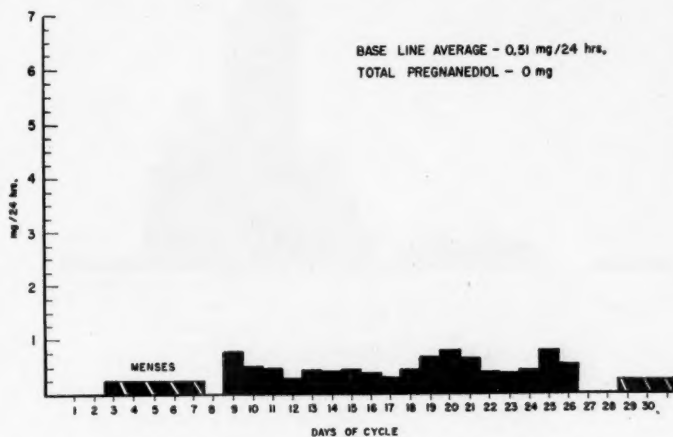
Case. 1.



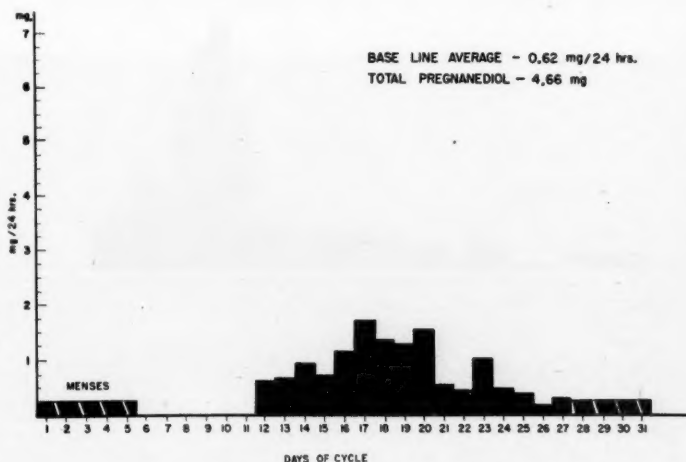
Case. 2.

CASE 2.—A 22-year-old married white woman, para ii, gravida ii, reported the onset of menses at the age of 11 years and rapid establishment of a regular cycle. The interval between periods varied from 26 to 30 days and menstrual flow was of 7 days' duration. Clots were infrequent and small. Cramps were moderate on the third day of menstruation. Premenstrual prodrome consisted of abdominal distention and an increase in gas with some looseness of stools. Pregnanediol was first detected in the urine on the sixteenth day and reached a maximum excretion point of 8.6 on the twentieth day of the cycle. Pregnanediol disappeared from the urine 48 hours prior to the onset of menstruation. The total quantity of pregnanediol excreted in the cycle was 27.37 mg.

CASE 3.—A 27-year-old single white woman reported the onset of menses at the age of 12 years and the rapid assumption of a regular cycle. The interval between periods varied from 22 to 26 days with the average flow of 5 days' duration. Clots were small and infrequent. Cramps were usually mild and confined to the first day of the period. During the period following this study, the patient reported that cramps were severe. Premenstrual prodrome consisted of sensitiveness and soreness of the breasts occurring 4 to 5 days before the onset of menses. Urine specimens were consistently negative for pregnanediol. To confirm our impressions of an anovulatory cycle, an endometrial biopsy was obtained on the twenty-sixth day of what subsequently proved to be a 29-day cycle. Microscopic examination failed to reveal anything more than a proliferative endometrium. No pregnanediol was detected in the urine in the remaining days of the cycle.



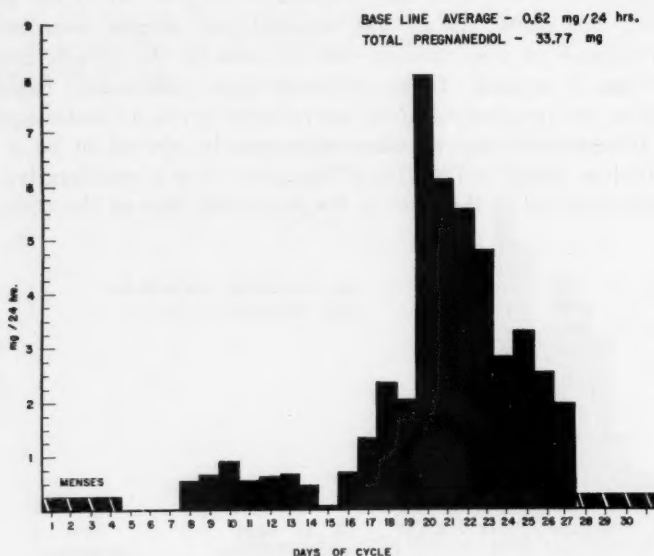
Case. 3.



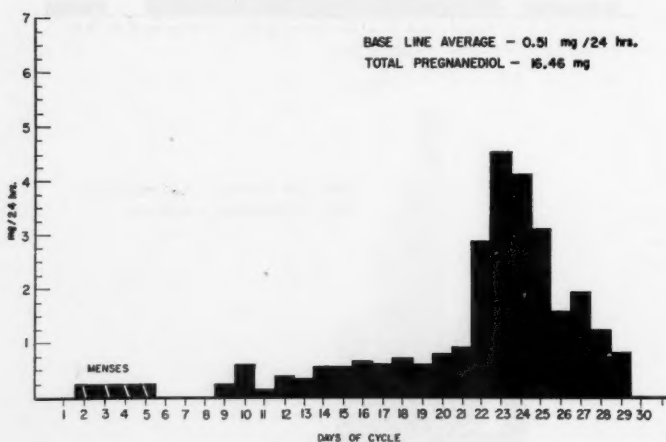
Case. 4.

CASE 4.—A 23-year-old single white woman reported the onset of menses at the age of 13 years. The usual interval between periods was 28 days with a flow of 5 days' duration. Clots were small and infrequent. Cramps were mild and confined to the first day of menstruation. The premenstrual prodrome consisted of occasional breast soreness and occasional distention of the abdomen. Pregnanediol was first detected in the urine on the fourteenth day and reached a maximum excretion of 1.75 mg. on the seventeenth day of the cycle. Although the value fell to the preovulatory levels on the twenty-first and twenty-second days of

the cycle, a significant quantity was found on the twenty-third day. No pregnanediol was detected for the remaining 4 days preceding the onset of the menstrual period. The total quantity of pregnanediol excreted during the period was 4.66 mg.



Case. 5.



Case. 6.

CASE 5.—A 32-year-old married white woman, para i, gravida ii, abortion i, reported the onset of menses at the age of 13 years. The usual interval between periods was 27 days with 3 to 4 days of menstrual flow. Clots and cramps were extremely rare. Pre-menstrual prodrome consisted of occasional breast soreness with rather consistent abdominal distention. Pregnanediol was first detected in the urine on the seventeenth day and reached a maximum excretion of 8.2 mg. on the twentieth day. Significant quantities of pregnanediol were still present on the day of the onset of menstruation. An endometrial biopsy was obtained on the twenty-sixth day of what subsequently proved to be a 28-day cycle. Microscopic examination confirmed the presence of definite progestational transformation. The total quantity of pregnanediol excreted in the cycle was 33.77 mg.

CASE 6.—A 24-year-old single white woman reported the onset of menses at the age of 13 years. The usual interval between periods was 28 days with 3 to 4 days of menstrual flow.

Clots and cramps had never occurred. Premenstrual prodrome consisted of breast soreness and abdominal distention. Pregnanediol was first detected in the urine on the twenty-first day and reached a maximum excretion of 4.6 mg. on the twenty-third day. A trace of pregnanediol was still present on the day preceding the onset of menstruation. The total quantity of pregnanediol excreted in the cycle was 16.4 mg.

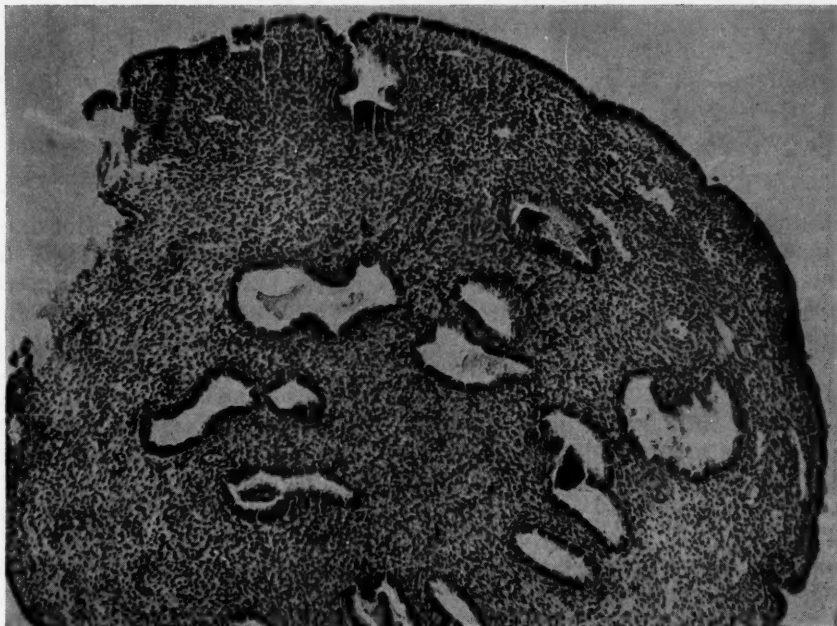


Fig. 1.—Endometrium obtained by biopsy in Case 3. Glands simple tubular and moderately dilated. No evidence of secretory activity was seen in any of the sections studied

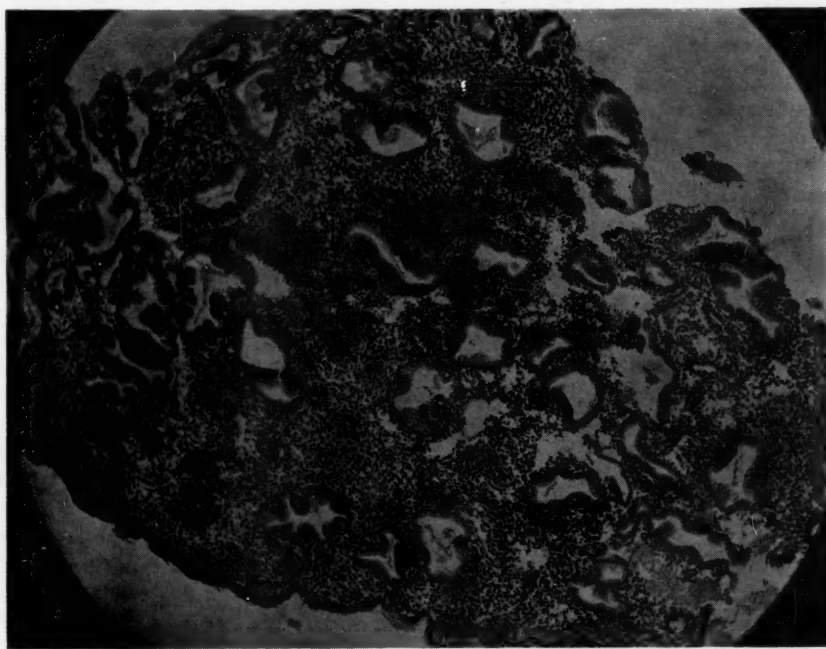


Fig. 2.—Endometrium obtained by biopsy in Case 5. Stroma edematous and glands tortuous. All sections showed secretory activity.

Our data, utilizing a new technique for free pregnanediol rather than the complex, have not revealed any material deviation from the original observations of Venning and Browne. It is noted, however, that in three of the cases presented, pregnanediol apparently has not disappeared from the urine at the time of the onset of menstruation. The amount of pregnanediol excreted during the cycles studied varied from 0 to 49.8 mg. per cycle. The pregnanediol appeared in the urine in unquestionable quantities from 10 to 13 days prior to the onset of menstruation. With the exception of Case 4, the maximum excretion occurred on the seventh or eighth day prior to the onset of the following menstrual period. In two of the cases presented, it was felt that ovulation had not occurred.

Comment

Venning and Browne¹¹ first submitted data on the pregnanediol excretion in the normal menstrual cycle using the method devised by Venning for the determination of the pregnanediol complex. The Venning data indicated that the excretion periods range from 6 to 12 days and the amount excreted per cycle varied from 3.0 to 54.6 mg. per cycle. These investigators also noted that the pregnanediol disappeared from the urine from 1 to 3 days prior to the onset of menstruation. Similar findings have been reported by investigators¹²⁻¹⁶ in this country and in Europe¹⁷⁻¹⁹ using the method of Venning. Some studies^{20, 21, 22} of the menstrual cycle are available that have utilized the Astwood-Jones technique for the determination of free pregnanediol. These have also conformed to the general pattern without any significant deviation from the data obtained by the Venning method. The only exception that we have demonstrated is the continued excretion of pregnanediol in definitely decreasing quantities at the time of onset of menstruation. Our clinical experience has not led us to suspect that it is necessary for progesterone production to cease before menstruation can occur. Hertz and Cromer²³ report that three patients receiving massive quantities of progesterone daily continued to menstruate regularly during a prolonged course of therapy. Segaloff²⁴ reported in 1949 that some patients who received smaller daily doses of progesterone showed no interference with the course of regular cycles of uterine bleeding.

Although the two endometrial biopsies subjected to study in the course of this investigation verified the assumptions based on pregnanediol excretion, it is not assumed that it could be demonstrated in all cases. In larger series studied in an attempt to correlate pregnanediol excretion with the histological changes in the endometrium, it has been indicated that proliferation may co-exist with the presence of the pregnanediol complex in the urine. Reinhart, Reel, and Shinowara²⁵ reported agreement in 87 per cent of 47 cases in which pregnanediol in the urine was associated with secretory activity of the endometrium. Other investigators²⁶ report that a stage of proliferation of the endometrium coexists with significant amounts of pregnanediol in the urine. Endometrial biopsies taken early in the luteal phase may, of course, show equivocal findings, as it is doubtful that progesterone present for only a matter of a few days is able to convert the proliferative endometrium into what we recognize as a typical progestational state. Hain and Robertson¹² report that pregnanediol was found in all of their cases in which a secretory endometrium could be demonstrated by biopsy obtained just prior to onset of menstruation. Although the exact status of this phenomenon is not yet settled, it is our opinion that detectable histological changes in the endometrium will be observed at the end of the luteal phase whenever pregnanediol appears in the urine during that phase of the cycle.

The authors wish to re-emphasize, as indicated by Wilson, Randall, and Osterberg,²⁶ that a normal menstrual history does not indicate the presence of

a normal physiological relationship of the hormones involved in the regulation of menstruation. There do not appear to be any significant clinical data to account for the discrepancies in the quantity of pregnanediol excreted during the cycles studied.

One point of interest which has arisen in the course of our study is worthy of further comment. In addition to the cases herein presented, 6 further cases have been subjected to investigation. In no instance has the greatest quantity of pregnanediol excreted by a single woman approached the least quantity excreted by a married woman. Although the number of patients is too small to have statistical significance, it is felt that this question is worthy of further exploration as it may indicate that differences may exist due to either hormonal activity in the seminal fluid or a neurogenic stimulus as a result of sexual activity.

Summary

1. Pregnanediol has been determined in the urine of 6 women during a normal menstrual cycle.
2. The quantity of pregnanediol excreted in this group ranged from 0 to 49.8 mg. with the maximum excretion occurring on the seventh day or eighth day of the cycle.
3. Pregnanediol excretion does not necessarily cease prior to the onset of menstruation.
4. It is emphasized that a normal menstrual history does not indicate normal physiological activity.

The authors wish to express their appreciation of the valuable technical assistance of Miss Martha Feldman and Miss Jane Egan.

References

1. Venning, E. H.: *J. Biol. Chem.* **119**: 473, 1937.
2. Astwood, E. B., and Jones, G. E. Seegar: *J. Biol. Chem.* **137**: 397, 1941.
3. Smith, O. W., Smith, G. Van S., and Hurwitz, D.: *AM. J. OBST. & GYNEC.* **51**: 411, 1946.
4. Davis, M. E., and Fugo, N. W.: *Proc. Soc. Exper. Biol. & Med.* **65**: 283, 1947.
5. Davis, M. E., and Fugo, N. W.: *Proc. Soc. Exper. Biol. & Med.* **69**: 436, 1948.
6. Summerville, T. F., Marrian, G. F., and Clayton, B. E.: *Lancet* **1**: 680, 1949.
7. Seitchik, Joseph: *AM. J. OBST. & GYNEC.* **60**: 877, 1950.
8. Smith, O. Watkins: *J. Clin. Endocrinol.* **10**: 496, 1950.
9. Smith, O. Watkins, and Schiller, S.: *Proc. Soc. Exper. Biol. & Med.* **73**: 378, 1950.
10. Chaney, A. L., McKee, W. E., Fischer, R. H., and McColgan, S. P.: *In press.*
11. Venning, E. H., and Browne, J. S. L.: *Endocrinology* **21**: 711, 1937.
12. Hain, A. M., and Robertson, E. M.: *Brit. Med. J.* **1**: 1226, 1939.
13. Heckel, G. P.: *New York State J. Med.* **42**: 2103, 1942.
14. Siegler, S. L., and Bauer, O.: *AM. J. OBST. & GYNEC.* **45**: 277, 1943.
15. Wilson, R. B., Randall, L. M., and Osterberg, A. E.: *AM. J. OBST. & GYNEC.* **37**: 59, 1939.
16. Stover, R. F., and Pratt, J. P.: *Endocrinology* **24**: 29, 1939.
17. Jayle, M. F., and Libert, O.: *Bull. Soc. chim. biol.* **28**: 372, 1946.
18. Riebold, G.: *Zentralbl. f. Gynäk* **64**: 2016, 1940.
19. Kaufmann, Carl, and Westphal, U.: *Klin. Wehnschr.* **24/25**: 910, 1947.
20. Jones, G. E. Seegar, Delfs, E., and Stran, H. M.: *J. Clin. Endocrinol.* **9**: 743, 1949.
21. Rogers, J., and Sturgis, S. H.: *J. Clin. Endocrinol.* **10**: 89, 1950.
22. De Watteville, H.: *J. Clin. Endocrinol.* **11**: 251, 1951.
23. Hertz, R., and Cromer, J. K.: *Symposium on Steroids in Experimental and Clinical Practice*, Philadelphia, 1951, The Blakiston Company.
24. Segaloff, A., Weed, J. C., Sternberg, W. H., and Parson, W.: *J. Clin. Endocrinol.* **9**: 1273, 1949.
25. Reinhart, H. L., Reel, P. J., and Shinowara, G. Y.: *Am. J. Clin. Path.* **11**: 219, 1941.
26. Wilson, R. B., Randall, L. M., and Osterberg, A. E.: *Proc. Staff Meet. Mayo Clin.* **13**: 197, 1938.

VARICOSE VEINS OF PREGNANCY

D. J. MULLANE, M.D., F.A.C.S., BOSTON, MASS.

(From the Vascular Clinic at the Boston Lying-in Hospital)

VERY little has been written about the treatment of varicose veins in pregnancy. Yet the problem is an important one, if for no other reason than its frequency. At the Boston Lying-in Hospital 11.2 per cent, or 1 in every 9 patients, are seen in the Vascular Clinic for the treatment of varicose veins. This is a relatively low incidence, for Siegler¹ states that 40 per cent of all pregnant patients are affected. Incidentally, he maintains that all pregnant patients will eventually develop varicose veins if they have a sufficient number of pregnancies. One patient has been seen in our clinic who developed varicose veins for the first time in her eleventh pregnancy.

Material

This is a study of 405 patients with varicose veins of varying degrees of severity. The material to be presented represents three years' experience with some selection. At first it seemed important to obtain information about a considerable number of patients, so that the figures would have statistical significance. After tabulating the patients seen in the first year and a half it became apparent that an insufficient number of patients was returning for follow-up evaluation. As a result, those patients who had been treated prenatally for varicose veins were more vigorously encouraged to return to the vascular clinic for a postpartum examination. Also, no record which did not contain a follow-up note was included in the statistics obtained from the second year and a half. In all, the records of 405 patients have been examined. The totals are sometimes less than this figure because all of the information was not always available in every record. The ages of the patients were tabulated (Table I). Twenty per cent of the patients were under 25 years of age. Thirty-five per cent were between 26 and 30 years of age, and 28.6 per cent were between 31 and 35 years of age. In all, 83.6 per cent of the patients were 35 years of age or under. This probably has no particular significance except to show the general age incidence of pregnancy patients in the prenatal clinic.

TABLE I. AGES OF PATIENTS STUDIED

	NUMBER	PER CENT
Under 21	10	2.5
21-25	68	17.3
26-30	142	35.2
31-35	115	28.6
36-40	53	13.2
Over 40	13	3.2
Total	402	100.0

Natural History

The natural history of varicose veins in pregnancy is a matter of some interest. They tend to be temporary, but become progressively larger and

more numerous throughout pregnancy. They tend to improve greatly after delivery, and they may even disappear completely. The latter is more likely to be the case if the current pregnancy is the first in which the abnormal veins have been apparent, and if they commenced late in the pregnancy. They reappear earlier in the next pregnancy. When they reappear they go on from where they left off in the last previous pregnancy. Eventually they become permanent varicose veins.

Most of the patients were not seen in the pregnancy in which their varicose veins started (Table II). Seventeen and six-tenths per cent of patients had some varicose veins before the first pregnancy; 30.6 per cent developed them during the first pregnancy. Another 28.3 per cent occurred for the first time in the second pregnancy, and 14.2 per cent in the third pregnancy. It will be noted that 76.5 per cent had developed varicose veins by the end of the second pregnancy, and 90 per cent by the end of the third pregnancy.

TABLE II. PREGNANCY IN WHICH VEINS STARTED

	NUMBER	PER CENT
Before first pregnancy	66	17.6
First pregnancy	115	30.6
Second pregnancy	107	28.3
Third pregnancy	53	14.2
Fourth pregnancy	23	6.1
Fifth pregnancy (or over)	12	3.2
Total	376	100.0

An attempt was made to determine in what part of pregnancy varicose veins were most likely to develop (Table III). Two hundred seventeen patients were able to remember the trimester in which the veins first appeared in the pregnancy of onset. The first and second trimesters are nearly equal, the third slightly less.

TABLE III. TRIMESTER OF ONSET OF VARICOSE VEINS IN PREGNANCY IN WHICH THEY FIRST APPEARED

	NUMBER	PER CENT
First trimester	81	37.3
Second trimester	86	39.6
Third trimester	50	23.1
Total	217	100.0

The pregnancy in which the patients were first seen in the Vascular Clinic is demonstrated in Table IV. Eighty-six per cent presented themselves for treatment during or before the fourth pregnancy. Most of them began treatment in the second trimester (Table V). On the other hand, the majority (70.4 per cent) of patients who had varicose veins in a previous pregnancy

TABLE IV. PREGNANCY IN WHICH PATIENTS FIRST PRESENTED THEMSELVES FOR TREATMENT

PREGNANCY	NUMBER	PER CENT
First	53	13.1
Second	113	27.9
Third	107	26.4
Fourth	77	19.0
Fifth or over (One patient was gravida xi.)	55	13.6
Total	405	100.0

developed recurrent veins in the first trimester in a subsequent pregnancy (Table VI). This group of 311 patients does not include those patients who had varicose veins even before the onset of the first pregnancy.

TABLE V. TRIMESTER FIRST SEEN

	NUMBER	PER CENT
First	42	10.4
Second	289	71.7
Third	72	17.9
Total	403	100.0

TABLE VI. TRIMESTER IN WHICH VEINS STARTED IN PRESENT PREGNANCY. DOES NOT INCLUDE PATIENTS WITH VARICOSE VEINS BEFORE THE FIRST PREGNANCY

	NUMBER	PER CENT
First trimester	219	70.4
Second trimester	89	28.6
Third trimester	3	1.0
Total	311	100.0

Etiology

There are at least three etiological factors in the development of varicose veins in pregnancy. Thirty-six and eight-tenths per cent of all subjects examined in a random series of autopsies of nonpregnant individuals had absent valves in the veins of one or both legs. The absence of valves may be considered the hereditary factor. In this group of patients 62 per cent had a family history of varicose veins (Table VII).

TABLE VII. PATIENTS WITH A FAMILY HISTORY OF VARICOSE VEINS

	NUMBER	PER CENT
Present	236	62.3
Absent	143	37.7
Total	379	100.0

Increased pressure inside the veins of the lower extremities during pregnancy has been demonstrated by the work of Veal and Hussey.² They measured the venous pressure in the popliteal vein of pregnant patients (some with varices and some without) and found that those who had varices also had a marked increase in venous pressure as compared with those who had none. All the patients with varices were between six and nine months pregnant.

The hormone factor remains to be proved. McCausland^{3, 4, 5} noticed a very low incidence of spontaneous abortion in pregnant patients with varicose veins. He deduced, from this observation, a high progesterone level. It has been our observation that increased symptoms in varicose veins may be the first sign of pregnancy. These symptoms have occurred before a menstrual period has been missed. We have attributed them to an unknown hormone effect.

Symptoms and Diagnosis

The symptoms of which these patients complain are fatigue, heaviness, and aching. Some have burning and cramps in the calf muscles at night. Many are partially incapacitated, and not a few are seriously incapacitated. The diagnosis is easily made on the basis of the typical appearance of dilated, tortuous, sacculated veins. There has been a popular fallacy that varicose

veins occur more frequently in one leg or the other. Information on this point was available in 399 records (Table VIII). Varicose veins are almost equally distributed between the right and the left leg with neither having any clear preponderance. Thirty-six and eight-tenths per cent had varicose veins in both legs.

TABLE VIII. LOCATION OF VARICOSE VEINS

	NUMBER	PER CENT
Right leg	131	32.8
Left leg	121	30.4
Both legs	147	36.8
Total	399	100.0

An attempt was made to estimate the severity in each instance (Table IX). Those veins which were relatively small, regardless of their extent, were called slight. Those which were large were called marked, and the remainder were called moderate. In this group 26 per cent were called slight, 62 per cent moderate, and 11 per cent marked. Forty-three patients, or 9.3 per cent, had vulval varices, and 1 patient had a varicose vein on the anterior surface of the cervix. Eighteen patients had had previous operations.

TABLE IX. SEVERITY OF VARICOSE VEINS

	NUMBER	PER CENT
Slight	104	26.2
Moderate	248	62.3
Marked	46	11.5
Total	398	100.0
Vulva	43	
Cervix	1	
Previous operation	18	

Treatment

In the past it has been customary to advise these patients to rest or to wear elastic bandages or stockings. At best they obtain only partial relief from these measures. The spread of the varicose system is uncontrolled. The purposes in treating varicose veins actively during pregnancy are:

1. To relieve symptoms;
2. To prevent the spread and stop the progressive development of varicose veins;
3. As a consequence, to prevent the development of permanent varicose veins;
4. To prevent spontaneous superficial phlebitis; and
5. To improve the appearance of the varicose veins.

The method we have been using is the injection of sclerosing solution into the lumen of the vein. No claim is made or implied that permanent major varicose veins can be cured by the injection treatment. The claim is made that most varicose veins can be relieved and controlled during pregnancy. The method is not new. It was suggested by McPheeters in 1931. It has been used and reported by Siegler, and by McCausland. It is a safe, effective, and simple office or clinic method of treatment. To date we have given over 10,000 such injections with no significant untoward reactions. In detail, injections should be started early—as early in pregnancy as possible—before symptoms are present, if possible, and in the pregnancy in which the veins first appear.

Injectations should be started at the top of the varicose system. A good occlusive reaction at the upper level will relieve the head of pressure on the veins below and give considerable prompt relief. Also, the patient should be standing so that the solution will flow downward and be well diluted before it finds its way into any deeper vessels. Subsequent injections are given at progressively lower levels.

The solution which we use is Monolate (monoethanolamine oleate). It is an effective, consistent solution giving moderate, satisfactory reactions. An occasional patient will develop an allergy to this solution. If that occurs a concentrated solution of sodium chloride and invert sugar is used for subsequent injections. Ordinarily one injection per leg involved is given at each visit. Sclerosing solutions must be given intravascularly. Extravascular injections cause painful sloughs which are slow to heal.

The dose per injection varies from 0.5 c.c. to 2.0 c.c. The smaller dose is used for small vessels and those veins feeding areas of dilated skin venules. Injections are given at weekly intervals. A pressure dressing of gauze and elastic adhesive is applied over the injection site, and allowed to remain for 24 hours. The patient is instructed to walk as much as possible for the first day or two following the injection. This tends to keep the discomfort at a minimum. Failure to keep active may result in a widespread reaction which is painful but otherwise of no great significance.

A tourniquet may be applied below the injection site if no reaction is otherwise obtainable or if the vein is very large. It is usually left in place for 10 minutes, and tends to confine the sclerosing solution to the injection site long enough to guarantee its effectiveness.

Injectations are discontinued when the patient has completed seven months of pregnancy to allow every reaction to be quiet and to remain so for some time before the patient is confined. Vulval varices are treated in the same way. Pressure is then obtained with a perineal pad instead of elastic adhesive.

This method of treatment does not and is not intended to supplant the necessary operative treatment of permanent, well-established, major varicose veins. Of 396 patients, 68.6 per cent received from 1 to 5 injections, 21.0 per cent received from 6 to 10 injections (Table X). The average total dose of sclerosing solution was 7.68 c.c. per patient.

TABLE X. NUMBER OF INJECTIONS GIVEN

	NUMBER	PER CENT
1-5	272	68.6
6-10	83	21.0
11-15	31	7.8
16-20	9	2.3
22	1	0.3
Total	396	100.0
Average total dose of sclerosing solution 7.68 c.c.		

Results

The immediate reactions were rated as good, slight, or none (Table XI). Eighty-nine and eight-tenths per cent of the patients developed good reactions at the site of the injection. Any reaction which could be palpated as a solid, cordlike, occluded vessel was rated as good. The remainder developed little or no reaction. The result of the treatment was estimated in each instance at the end of the course but before delivery (Table XII). Eighty per cent seemed to have a good immediate result; that is, the symptoms were relieved and the

leg had improved in appearance; 6 per cent had a poor immediate result and were obviously uncontrolled. Almost 11 per cent were considered to have had incomplete treatment because sufficient time for adequate treatment was not available. These were usually patients who presented themselves for treatment when they were as much as 6 months pregnant. Thirteen patients, or 3.3 per cent, had such obviously severe varices that injections were given only very briefly or not at all. These patients were operated upon prenatally.

Prenatal surgery in our limited experience is not uniformly successful. Usually the patient must be followed with injections for the balance of the pregnancy.

TABLE XI. IMMEDIATE REACTIONS

	NUMBER	PER CENT
Good	351	89.8
Slight	17	4.3
None	23	5.9
Total	391	100.0

TABLE XII. IMMEDIATE RESULT

	NUMBER	PER CENT
Good	317	80.0
Fair	4	1.0
Poor	20	5.0
Incomplete	42	10.7
Prenatal operation	13	3.3
Total	396	100.0

Follow-up notes were available on 231 of these patients (Table XIII). One hundred twenty-four, or 53.7 per cent, had no varicose veins and required no subsequent treatment. Seventy-seven, or 33.3 per cent, had only minor residual varices which were entirely obliterated by postpartum injections. The total, 87 per cent, obtained a good result eventually, without varicose veins, by injections alone. Actually, the percentage is probably higher because a number of patients seen in a subsequent pregnancy failed to return for follow-up due to their complete relief. Thirty patients, or 13 per cent, required postpartum operation, 9 of whom refused.

TABLE XIII. EVENTUAL RESULT

	NUMBER	PER CENT
Good (no injections)	124	53.7
Good (injections)	77	33.3
Postpartum operation	21	9.1
Operation advised (refused)	9	3.9
Total	231	100.0

The average number of postpartum injections given (Table XIV) was 2.5; the average total postpartum dose of sclerosing solution was 4.8 c.c. Uniformly larger doses of sclerosing solution may be given to the nonpregnant than to the pregnant patient, with much milder reactions. It seems significant that none of these patients developed a spontaneous superficial phlebitis following delivery, and only one developed a deep venous thrombosis (Table XV). She had a history of previous deep venous thrombosis and also had a previous operation for varicose veins.

TABLE XIV. POSTPARTUM INJECTIONS

Average number	2.5
Average total dose	4.8 c.c.

TABLE XV. SPONTANEOUS POSTPARTUM PHLEBITIS

Superficial	None
Deep	One

Summary

In summary, a series of 405 patients treated for varicose veins during pregnancy by the injection of sclerosing solution is presented.

The incidence, etiology, symptoms, distribution, purposes of treatment, and the details of treatment are discussed.

Eighty-seven per cent of those who returned for postpartum examination eventually obtained a good result by injections alone. Thirteen per cent required postpartum surgery.

No superficial thrombophlebitis was observed, and only one case of postpartum deep venous thrombosis.

References

1. Siegler, J.: Am. J. Surg. 44: 403, 1939.
2. Veal, J. R., and Hussey, H. H.: Surg., Gynec. & Obst. 72: 841, 1941.
3. McCausland, A. M.: West. J. Surg. 51: 199, 1943.
4. McCausland, A. M.: West. J. Surg. 47: 81, 1939.
5. McCausland, A. M.: California & West. Med. 50: 258, 1939.

1101 BEACON STREET

BLOOD SUGAR VALUES IN LABOR

J. BERNARD BERNSTINE, M.D., AND THEO. H. BOYSEN, III, M.D.,
PHILADELPHIA, PA.

(From the Department of Obstetrics and Gynecology, Jefferson Medical College)

INTRAVENOUS glucose has long been known to be of value to mothers in long or difficult labors, and in uterine inertia. Its beneficial effect on the babies of these mothers has also long been appreciated.

Cantarow and Trumper¹ reveal that the injected glucose, when absorbed, is brought to the liver and is changed, in large part, and stored there as glycogen. A relatively small proportion of the glucose may be utilized directly in the course of metabolic activity of the liver cells. The excess glucose which cannot be stored as glycogen or utilized directly by the liver, passes into the general circulation and is carried to the tissues where it is transformed into glycogen and stored as such in the muscles or it is utilized directly for energy.

The liver is capable of storing 150 to 200 Gm. of glycogen which constitutes the carbohydrate reserve which normally appears to be the sole direct source of sugar present in the blood stream.

That the maternal blood sugar is of considerable importance in obstetrics is evident as witnessed by the reports in the literature. However, most interest has been centered around the relationship of maternal blood sugar to that of the newborn.

Holman and Mathew² showed that in 50 cases the maternal blood sugar averaged 102 mg. per 100 c.c. while that of the offspring averaged 90.4 mg. per 100 c.c., both taken immediately at birth.

Kelleringham and Austin,³ in 50 cases, found the maternal blood sugar at birth (finger blood) to be 124.6 mg. per 100 c.c.

Most observers agree that maternal blood, at the time of delivery, has a higher blood sugar content than that found at any other time during the pregnancy.

We felt that an actual blood sugar determination study of patients in labor would shed considerable light on the supportive therapy of prolonged and difficult labors as well as aid in prophylactic treatment of the as yet unborn child, especially if that child be premature.

Morriss,⁴ in 1917, also found a higher blood sugar level at delivery than at any other time during the pregnancy and in addition found that in five cases he studied the blood sugar during labor was lower than at delivery.

Kelleringham and Austin,⁵ in 1938, in 28 cases found the mean blood sugar during the first stage of labor to be 93.4 mg. per 100 c.c. while in the same cases at delivery it was 121.8 mg. per 100 c.c.

Rowley,⁶ however, concluded from his studies that age, parity, long labor, and postpartum hemorrhage do not influence maternal blood sugar.

Material

It is the purpose of this paper to present the findings in a series of 105 labors and deliveries conducted on the Ward Obstetrical Service of the Jefferson Medical College Hospital during November, 1947, through January, 1948. Patients are grouped as to age, parity, medication received, length of labor, and as to toxemic manifestations. The blood sugar values for each are shown.

In addition, blood sugar values in 25 cases, taken during the seventh or eighth lunar month, are also presented.

All blood sugar specimens are nonfasting specimens. No selection of cases was intended. Specimens were taken from the median basilic vein of the woman when her pains occurred from three to five minutes apart lasting thirty to forty seconds. Ten c.c. of blood were drawn and placed immediately into test tubes containing a mixture of sodium fluoride and sodium oxalate. The oxalate acted as an anticoagulant while the fluoride prevented glycolysis if the analysis could not be done immediately. All specimens were taken immediately to the laboratory, if before five P.M., or placed in the icebox.

Protein-free filtrates were obtained and then the blood sugar determined, using the Benedict method and the colorimeter. Our laboratory uses a normal value of 60 to 100 mg. per 100 c.c.

All labors and deliveries were conducted by the intern and resident staff, who also secured the specimens. The hospital laboratory conducted the chemical determinations.

The specimens for women in the last trimester were taken from those who were registered in our Out-Patient Department. These were taken in the same manner, by the resident staff, during morning clinic hours, the time being between 10 A.M. and 11 A.M.

The past medical history of the first group (125 patients) revealed five cases of syphilis, one of cystitis, one of eclampsia, one of congenital syphilis, two of rheumatic fever, one of bronchial asthma, and one of renal disease.

One patient had a suburethral abscess, three had acute Neisserian infections of the cervix, one had pyelitis, one had contact ulcers of the labia (granulomatous), one had acute specific urethritis, five had positive Wassermann and Kahn tests, and three were Rh negative.

Table I shows the grouping of cases as to gravidity and their average blood sugars.

TABLE I

GRAVIDA	NUMBER OF CASES	AVERAGE BLOOD SUGAR MG. PER 100 C.C.
i	43	65.48
ii	20	74.40
iii	12	64.83
iv	9	69.22
v	10	71.80
vi	4	73.50
vii	4	65.25

The highest of 74.40 mg. and the lowest of 64.83 mg. shows very little significant difference as regards to gravidity.

Table II shows the grouping of cases as to age and their average blood sugars.

It will be noted that the lowest blood sugar values are in the lowest age group.

Table III shows the cases grouped as to length of labor with corresponding high, low, and average blood sugar values. A short labor included those from

one to four hours. A moderate labor included those from five to eighteen hours, and a prolonged labor included those of nineteen or more hours. All these are arbitrary standards.

TABLE II

AGE	NUMBER OF CASES	AVERAGE BLOOD SUGAR MG. PER 100 C.C.
15-20 years	35	64.57
21-25 years	33	68.54
26-30 years	19	70.26
31-35 years	14	70.85
36-40 years	4	71.25

TABLE III

LABOR	NUMBER OF CASES	BLOOD SUGAR MG. PER 100 C.C.		
		HIGHEST	LOWEST	AVERAGE
Short	10	89	50	63.90
Moderate	70	148	35	70.72
Prolonged	22	98	15	64.77

The low of 15 mg. per 100 c.c. in the prolonged labor group is the figure reported by the laboratory and is here reported. We realize the impracticability of this figure. This patient had a labor of 39 hours and 5 minutes. Two blood sugar determinations were taken. The first specimen was taken 27 hours before delivery and showed 64 mg. per 100 c.c. The second specimen (the doubtful one) was taken 2¼ hours before delivery. This woman received 10 per cent glucose in water following the second specimen.

Three case histories did not reveal the length of labor so they are not included in Table III.

Four cases were occiput posterior positions and one a frank breech with nuchal position of the arms. There were four cases of moderate postpartum hemorrhage and one that required manual removal of the placenta.

There were no noteworthy maternal complications observed during the puerperium.

Twelve cases of prematurity were encountered and Table IV lists them with gravidity, weight of baby, length of labor, and blood sugar values.

TABLE IV

CASE NO.	GRAVIDA	WEIGHT OF BABY POUNDS OUNCES		HOURS OF LABOR HOURS MINUTES		BLOOD SUGAR MG. PER 100 C.C.
8	ii	4		6		72
5	iii	5	2	10	11	71
21	vi	4		15	30	95
26	i	4	5½	12	33	57
38	ii	5	6	8	50	95
46	ii	4	8	8	14	57
68	v	5	1	13	57	68
74	?	5	4½	8		70
81	ii	5	½	33		98
92	iii	5	5	5	20	35
98	i	5	7	18	15	67
1	ii	4	14	?		73

This group had a blood sugar average of 71.50 mg. per 100 c.c.

We feel that intravenous glucose is beneficial to these premature babies and should be administered to their mothers in labor.

Eight patients were classified as pre-eclampsies. Their highest blood sugar was 99 mg., lowest 54 mg., and average 70.12 mg.

TABLE V

CASE NO.	MEDICATION MG. OR GR.	TIME GIVEN	TIME OF DELIVERY	BLOOD SUGAR MG. PER 100 C.C.	TIME OF BLOOD SUGAR DETERMINA- TION	LENGTH OF LABOR	
						HOURS	MINUTES
1	*Dem. 50 †Scop. $\frac{1}{200}$	1:30 P.M.	3:02 A.M.	73	11:20 P.M.	21	
2	Dem. 50	2:00 A.M.	2:10 A.M.	57	9:30 P.M.	10	14
5	Dem. 50	5:15 A.M.	8:03 A.M.	71	7:00 A.M.	10	11
7	Dem. 50	9:00 A.M.	10:15 A.M.	57	7:00 A.M.	7	30
8	Dem. 50	7:00 A.M.	8:49 A.M.	72	7:00 A.M.	6	5
10	Dem. 50	12:45 A.M.	3:00 P.M.	15	12:45 A.M.	39	5
	Dem. 50	11:20 A.M.					
	Dem. 100	2:15 P.M.					
11	Dem. 50	2:20 P.M.		73		8	35
	Scop. $\frac{1}{150}$						
	Dem. 50	4:30 P.M.					
	Scop. $\frac{1}{200}$						
12	Dem. 50	2:45 P.M.	5:47 P.M.	86	2:00 P.M.	12	6
14	Dem. 50	8:50 A.M.	1:00 P.M.	60	10:00 A.M.		
15	Dem. 50	9:30 A.M.	9:35 P.M.	88	9:30 A.M.	20	40
17	Dem. 50	8:30 P.M.	7:08 P.M.	68	9:00 A.M.	18	15
	Scop. $\frac{1}{150}$						
	Dem. 50	9:00 A.M.					
	Gwathmey	12 NOON					
19	Dem. 100	12 MID.	4:08 A.M.	75	3:00 A.M.	7	55
21	Chloral hy. gr. xxx	3:00 P.M.	3:50 P.M.	95	2:00 P.M.	15	30
22	Dem. 100	4:45 P.M.	8:47 P.M.	71	8:00 P.M.		
	Scop. $\frac{1}{150}$						
23	Dem. 50		9:11 P.M.	62	7:45 P.M.	14	
28	Dem. 50	1:15 P.M.	6:15 A.M.	52	4:45 A.M.	33	25
29	Dem. 50	11:00 A.M.	12:02 P.M.	90	11:00 A.M.	13	20
	Scop. $\frac{1}{150}$						
30	Dem. 50	12:30 A.M.	7:57 P.M.	88	10:40 A.M.	30	13
	Dem. 50	8:45 A.M.					
31	Dem. 50	12:30 P.M.	10:30 A.M.	76	8:30 P.M.	31	
	Dem. 100	11:00 P.M.					
	Dem. 50	8:45 A.M.					
32	Chloral hy. gr. xxx	2:00 P.M.	3:50 A.M.	99	9:00 P.M.	7	35
33	Dem. 50	8:50 A.M.	1:35 P.M.	72	8:15 A.M.	26	
	Gwathmey	11:30 A.M.					
35	Dem. 100	12 MID.	7:53 A.M.	85	9:40 P.M.	61	20
	Scop. $\frac{1}{150}$						
36	Dem. 50	9:00 A.M.	11:29 A.M.	76	10:15 A.M.	17	29
38	Dem. 50	9:30 A.M.	11:54 A.M.	95	10:15 A.M.	8	50
41	Dem. 100	4:30 A.M.	12:15 P.M.	61	1:00 A.M.	18	15
	Dem. 100	8:45 A.M.					
42	Dem. 100	12:20 P.M.	6:30 P.M.	66	9:40 A.M.	27	
43	Dem. 50	8:30 A.M.	1:35 A.M.	62	10:50 A.M.	3	12
44	Dem. 50		5:26 A.M.	71	1:00 A.M.	7	56
46	Dem. 50		8:10 A.M.	57	12:45 A.M.	8	14
47	Dem. 50	9:10 A.M.	1:18 P.M.	64	9:07 A.M.	12	29
	Dem. 100	9:10 A.M.					
48	Dem. 50	6:30 P.M.	7:30 P.M.	75	6:00 P.M.	9	45
49	Dem. 50	9:30 P.M.	12:17 A.M.	80	11:45 A.M.	10	26
	Sod. Pento- barb. gr. III	12:20 P.M.					
	Dem. 50	6:30 A.M.					
50	Dem. 50	4:00 P.M.	6:51 P.M.	74	4:30 P.M.	18	
55	Dem. 100	11:30 A.M.	1:08 P.M.	80	11:45 A.M.	5	
56	Dem. 100	4:30 P.M.	7:03 P.M.	100	4:00 P.M.	14	
57	Dem. 100	12:05 A.M.	4:55 A.M.	64	4:00 A.M.	13	6
	Dem. 100						

TABLE V—CONT'D

CASE NO.	MEDICATION MG. OR GR.	TIME GIVEN	TIME OF DELIVERY	BLOOD SUGAR MG. PER 100 C.C.	TIME OF BLOOD SUGAR DETERMINATION	LENGTH OF LABOR HOURS MINUTES	
58	Dem. 50	5:50 A.M.	6:43 A.M.	76	5:25 A.M.	23	
	Dem. 100						
59	Dem. 100	10:00 P.M.	12 NOON	47	4:05 P.M.		
	Dem. 100	4:00 A.M.					
	Pentobarb. gr. III	5:45 A.M.					
60	Dem. 50	8:45 P.M.	9:58 P.M.	38	9:00 P.M.	38	45
61	Dem. 50	12:30 P.M.	4:41 P.M.	43	4:30 P.M.	8	33
69	Dem. 50	6:00 A.M.	7:29 P.M.	68	9:00 A.M.	23	10
	Dem. 100	10:50 A.M.					
	Scop. $\frac{1}{150}$						
	Dem. 100	6:50 P.M.					
	Scop. $\frac{1}{150}$						
71	Dem. 50	8:15 A.M.	9:15 A.M.	81	8:15 A.M.	9	15
72	Dem. 100	8:45 P.M.	10:05 P.M.	58	8:50 A.M.	50	34
73	Dem. 100	1:30 P.M.	4:34 P.M.	58	1:45 P.M.	8	30
75	Dem. 100	8:00 A.M.	1:52 P.M.	60	12:40 P.M.	53	4
	Scop. $\frac{1}{150}$						
	Dem. 50	12 NOON					
77	Dem. 50	8:45 P.M.	7:15 P.M.	57	5:10 P.M.	21	
78	Dem. 50	4:15 P.M.	9:45 P.M.	66	4:55 P.M.	13	45
82	Dem. 50	3:45 P.M.	5:08 P.M.	61	3:15 P.M.	8	45
84	Dem. 50	2:30 P.M.	4:42 P.M.	30	2:15 P.M.	36	
86	Dem. 50	5:05 A.M.	7:07 A.M.	66	5:15 A.M.	20	
88	Dem. 50	11:40 P.M.	12:20 A.M.	55	11:55 P.M.	9	50
89	Dem. 50	5:25 P.M.	11:18 P.M.	54	6:45 P.M.	22	30
	Dem. 100	9:00 P.M.					
	Scop. $\frac{1}{150}$						
93	Dem. 50	5:30 P.M.	10:25 P.M.	58	6:55 A.M.	20	30
	Scop. $\frac{1}{150}$						
94	Dem. 50	12:15 P.M.	2:23 P.M.	43	11:45 A.M.	8	27
	Dem. 50	2:00 P.M.					
	Scop. $\frac{1}{200}$						
95	Dem. 100	10:55 P.M.	5:25 A.M.	148	12:45 A.M.	13	53
	Scop. $\frac{1}{150}$						
	Dem. 100	12:45 A.M.					
	Scop. $\frac{1}{150}$						
98	Dem. 50	9:30 A.M.	12:42 P.M.	67	9:30 A.M.	18	15
99	Dem. 50	12 NOON	2:08 P.M.	62	12 NOON	6	50
100	Dem. 100	12:25 P.M.	2:46 P.M.	58	11:15 A.M.	10	52
	Scop. $\frac{1}{150}$						
101	Dem. 50	2:00 P.M.	6:50 P.M.	53	2:00 P.M.	11	17
102	Dem. 50	4:30 P.M.	5:28 P.M.	50	4:30 P.M.	1	15
104	Dem. 50	7:25 P.M.	9:32 P.M.	64	7:30 P.M.	5	37
105	Dem. 50	5:30 P.M.	7:58 P.M.	52	5:30 P.M.	4	50

*Dem. = Demerol.

†Scop. = Scopolamine.

Forty-two patients received open-drop ether with pains plus local infiltration with Metycaine for episiotomy repair. Eight received continuous spinal anesthesia for delivery. Two received pudental block. Eleven received moderate ether anesthesia. Two received nitrous oxide-oxygen mixture and thirty-seven received local infiltration only.

No attempt is made to show relationship of anesthesia to blood sugar as specimens were taken before anesthesia was administered.

Table V shows the relationship between premedication, time given, time of delivery, amount of blood sugar, time of blood sugar determination, and length of labor.

We fail to find any significant correlation between the various factors mentioned.

In Table VI those babies who weighed 8 pounds or more, along with length of labor and amount of blood sugar, are shown.

TABLE VI

CASE NO.	WEIGHT OF BABY		BLOOD SUGAR MG. PER 100 C.C.	LENGTH OF LABOR	
	POUNDS	OUNCES		HOURS	MINUTES
3	10	8	57	8	10
4	8	2½	65	7	30
11	8	13	73	8	35
13	8	6½	89	3	12
14	8	2	60		
20	8	6¼	83	20	50
22	8	5½	71		
23	8	8¼	62	14	
32	8	2½	99	7	35
40	8	14	80	11	6
44	8		71	7	56
54	8	7	54	10	45
55	8	½	80	5	
57	9	10	64	13	16
59	8	9½	47		
66	9	2	62	7	34
72	8	14¾	58	50	34
86	8	4	66	20	
89	8	10½	54	22	30
94	8	2	43	8	27
95	8		148	13	33

Although there have been reports showing relationship between high blood sugar values and large babies, these results show no significant correlation.

Of the twenty-five cases in which determinations were taken during the seventh or eighth lunar month, the highest value was 111 mg. per 100 c.c. The average was 81.52 mg. per 100 c.c.

Mays and McCord⁷ state the blood sugar concentration probably depends upon the patient's nutritional state and the degree of emotional stability and muscular activity immediately preceding the taking of the specimen.

Morriss⁸ says maternal blood sugar values are high at birth because of the voluntary muscular effort, the wrought-up mental state of the patient, and the anesthesia.

We subscribe to the above two statements with slight reservation.

Summary and Conclusions

In a study of this kind there are so many variable factors that conclusions are difficult to draw. One has no definite idea of the nutritional state of these patients on admission, nor what it was during the past week. Hence, one's estimate of the glycogen reserve is not too accurate.

However, that the average blood sugar is lower in labor than during the prenatal course is shown by our studies. That there is any relationship between low blood sugar, premedication, length of labor, or size of child is difficult to say at this time.

We do feel that the administration of glucose intravenously during labor in anticipated difficult cases and prolonged labor is efficacious as it gives immediate fuel for consumption and enhances the glycogen reserve. Glucose is beneficial to the unborn child, especially when the child is premature.

One hundred five cases of labor and delivery have been presented according to gravity and blood sugar; length of labor and blood sugar; pre-eclamptic state and blood sugar; premedication, length of labor, and blood sugar; weight of baby, length of labor, and blood sugar.

In addition the blood sugar levels of twenty-five prenatal patients at about thirty weeks' gestation are also presented.

References

1. Cantarow, A., and Trumper, M.: *Clinical Biochemistry*, Philadelphia, 1945, W. B. Saunders Company.
2. Holman, A. W., and Mathew, A.: *AM. J. OBST. & GYNEC.* **25**: 138, 1933.
3. Kelleringham, R. C., and Austin, B. R.: *Am. J. M. Sc.* **195**: 318, 1938.
4. Morriss, W. H.: *Bull. Johns Hopkins Hosp.* **28**: 140, 1917.
5. Kelleringham, R. C., and Austin, B. R.: *Am. J. M. Sc.* **195**: 318, 1938.
6. Rowley, W. N.: *AM. J. OBST. & GYNEC.* **5**: 23, 1923.
7. Mays, C. R., and McCord, Wm.: *AM. J. OBST. & GYNEC.* **29**: 405, 1935.
8. Morriss, W. H.: *Bull. Johns Hopkins Hosp.* **28**: 140, 1917.

255 SOUTH 17TH STREET

FEVER IN ENDOMETRIOSIS*

ISADOR FORMAN, M.D., PHILADELPHIA, PA.

(From the Department of Obstetrics and Gynecology, Temple University Hospital)

PELVIC endometriosis produces many and varied symptoms. Acquired dysmenorrhea, abnormal uterine bleeding, backache, and dyspareunia, are the classic ones.

Although, other, less frequently encountered symptoms are described in the reports of this increasingly important disease, fever is seldom mentioned as one of them.

Scott and Te Linde,¹ in a recent review of 516 cases of proved endometriosis, encountered such unusual symptoms as headache, swollen ankles, indigestion, flank pain, general fatigue, rectal bleeding, and hematuria. Fever is not mentioned.

The classic contributions of Keene and Kimbrough,² Counsellor,^{3, 4} Payne,⁵ Fallas and Rosenbloom,⁶ and Meigs⁷ describe the pathology, symptomatology, diagnosis, and treatment of endometriosis in minute detail, but none of these reported the presence of fever.

W. R. Holmes⁸ reported 80 cases of endometriosis of which seven, or 8.7 per cent, had a temperature elevation and leukocytosis. Jeffcoate⁹ in 1947 reported 8 instances of fever occurring in 91 cases of proved endometriosis which were operated upon.

Our interest in this symptom, in relation to endometriosis, began in 1945. Since that time, five cases in which fever was a prominent symptom of this disease have come under our observation. Three of these were operated upon and form the basis of this report.

Case Reports

CASE 1.—Mrs. E. E., aged 32 years, married 3 years, with no pregnancies, was admitted to the hospital on Oct. 18, 1945, with a chief complaint of pain in the back radiating down both legs. She was well until 3 months ago when she developed severe backache radiating down both thighs. No disturbance in gait, no subjective sensory disturbances. The menstrual history was not recorded (patient admitted on medical service).

She had had a left ovarian cystectomy and appendectomy in 1942.

Physical Examination.—Negative except for marked right costovertebral angle tenderness. Blood pressure was 110/80.

Admitting Diagnosis.—Chronic right pyelonephritis with perinephritis. Pelvic adhesions.

Laboratory Findings.—Urinalysis of catheterized specimen was negative; red blood count, 4,750,000; hemoglobin, 13.5 Gm.; white blood count, 5,600; neutrophils, 66 per cent; lymphocytes, 31 per cent; monocytes, 2 per cent; basophiles, 1 per cent; urine culture, negative for tuberculosis; feces examination, negative for blood and parasites.

*Presented at a meeting of the Philadelphia Obstetrical Society Oct. 4, 1951.

X-ray Findings.—Oct. 17, 1945, "Barium enema shows colon to be essentially negative. Multiple filling defects can be attributed to gas and feces. But, because of these shadows, polyps cannot be excluded."

Oct. 18, 1945, "Intensified oral cholecystography demonstrates a normally functioning gall-bladder without stones."

Oct. 19, 1945, "Chest grossly negative fluoroscopically. Esophagus negative, stomach negative, duodenum and small intestine, essentially negative."

Oct. 22, 1945, "Intravenous urography shows no definite evidence of pathology in kidney pelves or ureters. Slight asymmetry in size and configuration of kidney pelves is difficult to evaluate, since they may be within physiologic limits. However, we are inclined to suspect that there has been some previous obstructive uropathy on the right, although none is demonstrated at present. Reexamination at a later date for evidence of further change or persistence of the present findings is suggested, if no cause for the patient's symptoms is found."

On October 29 a gastroenterologist saw the patient and reported the following, "I felt a nodule, perhaps the size of a large chestnut, through the anterior rectal wall, evidently high in the pouch of Douglas. This was exquisitely tender and could only be felt when the patient strained. This arouses the suspicion of a metastatic implant. Sigmoidoscopic examination discloses no mucosal lesion in the location of palpated nodule. Gynecologic examination indicated." (H. L. Bockus.)

Pelvic examination on October 30, "Vulva and vagina normal. Cervix small, conical and well epithelized. Corpus normal in size, anterior, somewhat limited in mobility. Left adnexa not palpated. Right ovary slightly enlarged and tender. Both utero-sacral ligaments thickened with a tender nodule on the left."

"Impression.—Pelvic endometriosis.

"In view of the patient's age, her desire for children, and the minimal pelvic pathology, a trial of conservative therapy (androgen therapy) is suggested."

During this period of observation and study, the patient's temperature fluctuated between 98.6 and 100.2° F. There was a daily afternoon rise. The patient was discharged from the hospital to the care of her physician who prescribed testosterone 25 mg. daily.

She was readmitted to the hospital on Feb. 13, 1946. The following admission note was made. "On testosterone 25 mg. daily since discharge from the hospital. On testosterone therapy until January 7. Under this treatment, temperature came down to normal, pain much relieved, gained ten pounds in weight. Pain and fever recurred two weeks after stopping testosterone therapy. The two months, during which she was on testosterone therapy, was the first time her afternoon temperature was normal in 18 months."

X-ray Examination.—"Barium enema shows the colon to be essentially negative. There is, however, a suspicious indentation on the anterior aspect of the recto-sigmoid which could be due merely to angulation of the bowel but the possibility of encroachment by an endometrial mass should be considered, in view of the clinical findings."

On Feb. 20, 1946, Dr. Bockus reported: "The nodule previously palpated seems to be approximately one-half its previous size and I suspect it is not quite as firm in consistency. The sigmoidoscope examination again failed to reveal mucosal involvement."

The patient was discharged from the hospital on February 22. Her temperature had fluctuated between 98.3 and 99.6° F. during her hospital stay.

She was readmitted on Sept. 22, 1946, this time to the gynecologic service.

The following is the admission note: "Catamenia 13 × 28 × 3-5, L.M.P., 9/2/46. For the past 3 years patient has had severe intermittent attacks of low back pain. The pain has a definite relationship to the menstrual cycle. Relieved usually following menstrual flow, starts about midcycle with increasing intensity as the period starts. She has received a thorough orthopedic, x-ray, G.I. and gynecologic investigation in the past, with a final diagnosis of endometriosis. Patient did respond to testosterone therapy but appearance of masculinizing symptoms made her discontinue treatment." The temperature was 99.4° on admission.

A subtotal hysterectomy and bilateral salpingectomy and right oophorectomy were performed by Dr. R. A. Kimbrough, who made the following operative note: "A few small

omental adhesions were found on excision of previous scar and separated. The right ovary enlarged to three times normal size by several cysts containing dark blood. An area of endometriosis was found on anterior rectal wall just above pelvic floor and several small implants in peritoneum of anterior cul-de-sac. A supravaginal hysterectomy and bilateral salpingectomy and right oophorectomy performed."

Pathologic Findings.—The uterus minus the cervix was 5.5 cm. by 5.5 cm. by 4 cm. thick. The wall was 2 cm. thick and the endometrium was 5 mm. thick. There was a small intramural fibroid 9 mm. in diameter. There were two Fallopian tubes and one ovary. The fimbriated extremities of the tubes appeared to be open. The ovary was fairly smooth surfaced and measured 4.5 by 3.5 by 2.3 cm. It contained two good-sized cysts, one 2 cm. in diameter.

Microscopy: Endometrium, interval stage; small tumor, leiomyoma; Fallopian tubes, not diseased; ovary: there is a small cyst containing blood and lined with columnar epithelium, but not typical of endometrium.

The patient made an uneventful postoperative recovery and when she was last seen, on June 13, 1950, stated that she had been completely relieved of all her symptoms following operation.

CASE 2.—Mrs. M. S., aged 34 years, married 9 years, was admitted to the hospital Oct. 18, 1945, with the chief complaint of pain in the left lower quadrant. The patient had been well until 6 years ago, when she began to experience lower abdominal pain and dysmenorrhea. She was always aware of discomfort in the pelvis but during her periods the pain became severe and, at times, incapacitating. In the past two years, she had received injections of Dilaudid during these attacks. There had been a weight loss of 24 pounds, during this period. There was no vaginal discharge.

Menstrual History.—Onset at age 21 years, regular, 30-day cycle, until two years ago when periods recurred every 23 to 25 days, became more profuse and painful. Last menstrual period began on Oct. 13, 1945.

There was a history of swollen cervical glands in childhood. She had always been rather sickly and underweight.

Physical Examination.—This revealed a rather pale, thin, anxious-looking white woman. Her weight was 84 pounds. Temperature 100.4° F. on admission, blood pressure 96/64, pulse 92, and respirations 20. Head, neck, and chest were negative. The abdomen was scaphoid with no scars, no masses palpated. There was marked tenderness in both lower quadrants, more marked on the left.

Pelvic Examination.—Vulva and vagina were normal. The cervix conical and well epithelized, the corpus was enlarged to the size of an 8-week pregnancy and limited in its mobility by a firm, tender, 4 cm. mass in the region of the left ovary. The right tube and ovary seemed normal.

Rectovaginal Examination.—Confirmed the above and revealed some induration in the cul-de-sac.

Laboratory Studies.—Urinalysis showed a very faint trace of albumin, otherwise negative; serology, negative; hemoglobin, 11 Gm.; red blood count, 3,750,000; white blood count, 12,600; polymorphonuclear leukocytes, 77 per cent; lymphocytes, 22 per cent; fasting blood sugar, 112.

Chest Roentgenogram.—There was no evidence of pulmonary pathology.

The temperature rose daily to 100.2° F. and one afternoon reached 100.8° F., during the five days of observation.

Endometriosis was considered a logical diagnosis but in view of the patient's habitus and low-grade fever the presence of tuberculous salpingitis was considered more likely.

A laparotomy was performed on Oct. 23, 1945. The abdominal viscera and appendix were normal. The uterus was enlarged, with two small myomatous nodules in the region of the left cornu. The left tube and ovary were densely adherent in the cul-de-sac and dissection of these structures left a raw, oozing surface on the peritoneum covering the left uterosacral ligament. A supracervical hysterectomy was performed. The temperature came down to normal on the fifth postoperative day and remained so until discharge one week later.

Pathologist's Report.—"Gross pathology—myomata of uterus. Sections showed myomata of uterus, few areas of adenomyosis, hyperplasia of endometrium, no evidence of malignancy."

The patient has remained symptom-free since operation and, when last examined, on Sept. 21, 1947, had gained 35 pounds in weight.

CASE 3.—Mrs. D. B., aged 32 years, married 8 years, was admitted to the Temple University Hospital on Nov. 7, 1949, with chief complaints of backache, left lower quadrant pain, and increase in the menstrual flow.

She had been in fairly good health until 15 months ago when she began to experience dysmenorrhea and an increase in the menstrual flow. Soon afterward she developed almost constant backache and rectal pressure. In recent weeks, she noticed a feeling of warmth during the late afternoon and evening.

Past History.—In 1943 she was operated upon for acute appendicitis but, at operation, it was found she had a ruptured hemorrhagic cyst of the left ovary. An appendectomy and left salpingo-oophorectomy were performed. In June, 1949, a hemorrhoidectomy was performed.

Menstrual History.—Onset was at age 15 years, every 23 days, lasting 3 to 5 days, painful during the past three years. Her last menstrual period was on Oct. 24, 1949. She had never been pregnant. Contraceptives were used until four years ago.

Physical Examination.—She was a rather pale, slight, young white woman, weighing 96 pounds. Blood pressure was 104/60, pulse 90, temperature 100.2° F. The breasts were small and flaccid, no masses. The abdomen was marked by a long right lower quadrant scar, with no masses palpable; there was some tenderness on deep pressure in the right inguinal region.

Pelvic Examination.—The vulva and vagina were normal; the cervix was conical and smooth; the corpus was retroverted and nodular and tender; there was a 6 cm. cystic mass in the region of the right ovary.

Provisional Diagnosis.—Pelvic endometriosis.

At the end of a four-day observation period, during which time her temperature reached 100° F. every afternoon, the patient was operated upon.

Operative Findings.—Through a median suprapubic incision, the pelvic viscera were exposed. The uterus was found to be retroverted and densely adherent to the rectosigmoid. There were dense adhesions between the uterus and a dark, thick-walled ovarian cyst, prolapsed into the cul-de-sac. The left adnexa were missing. A panhysterectomy and right salpingo-oophorectomy were performed.

Pathologist's Report.—Gross description, "The specimen consists of the entire uterus with one tube and ovary attached. The uterus measures 7 by 4 by 3 cm. The outer surface presents areas of roughening. The myometrium measures 1 cm. in thickness and is homogeneous. The endometrium measures 2 mm. The cavity is not dilated. The endocervical canal is patent and trabeculated. There is a superficial erosion at the external os. The uterine tube measures 6 by 1 cm. The surface is roughened and there are adhesions to the ovary. The ovary measures 4 by 3 by 2 cm. There is a 1.5 cm. hemorrhagic corpus luteum cyst. There are several small brownish areas noted on the surface of the uterus and at the junction of the tube and uterus, where sections were taken."

Microscopic Findings.—"The endometrium is in the non-secretory phase. One portion of tissue beneath the serosa shows a nest of stroma containing endometrial glands in the non-secretory phase. The ovary shows old corpora albicantia. The uterine tube shows recent hemorrhage (perhaps of traumatic nature)."

Diagnosis.—Endometriosis (serosa of uterus). Nonsecretory endometrium. Chronic cervicitis.

The patient made a good recovery. She was asked to take her temperature every afternoon for six weeks, postoperatively. During this period there were four readings above 98.6° F. The patient has remained well except for moderate hot flushes which were controlled with estrogens. Her last follow-up visit was Nov. 16, 1950.

During the past two years twelve patients, who have been labeled with a presumptive diagnosis of endometriosis, were asked to keep daily records of their afternoon temperatures. Two of these patients showed temperatures well above normal.

CASE 4.—Mrs. B. M., aged 36 years, married 9 years, with no pregnancies, was first seen on April 12, 1947, because of increasing dysmenorrhea.

The patient stated that she had always had some pain at her periods but during the past two years the condition had become much worse. A curettage and insertion of stem pessary were performed in 1946. No relief followed this procedure. She was advised to have a hysterectomy for a uterine tumor. The patient would not accept this advice.

Past History.—Irrelevant.

Menstrual History.—Onset was at 12 years, regular, every 26 days, 6 to 7 days in duration. She always had pain on the first day, but since onset of present condition, the pain was more severe and lasted 4 to 5 days.

Physical Examination.—Negative.

Pelvic Examination.—Vulva and vagina were normal. The cervix was negative; the corpus retroverted, "roughened," and seemed enlarged. Both adnexa were thickened and tender. The uterosacral ligaments were nodular and tense.

Provisional Diagnosis.—Pelvic endometriosis.

The patient refused surgery and has had considerable relief of symptoms by androgen therapy. She was asked to keep a chart of her daily 4 P.M. and 6 P.M. temperature readings. The temperature during the next two months ranged between 99 and 99.6° F., reaching 100° on four occasions. Although the dysmenorrhea was relieved by the administration of 20 mg. Oreton (buccal tablets) daily, the fever seemed uninfluenced.

CASE 5.—Miss B. R., aged 30 years, had a chief complaint of dysmenorrhea and pain in lower right quadrant.

The patient had always had moderate dysmenorrhea since the onset of menstruation at the age of 13 years. The pain became rather severe in 1945 and after a trial of various medical treatments, the patient was operated upon in December, 1946. At operation, an adherent retroversion was freed and the uterus suspended. The Fallopian tubes seemed normal. The dysmenorrhea was considerably relieved for about two years. In 1948, the pain at the period again became very annoying and there developed some backache and intermittent dull right lower quadrant pain.

Physical Examination.—General examination was negative. The abdomen showed a well-healed lower midline scar.

Pelvic Examination.—Vulva and vagina were negative. The cervix was slightly eroded, the corpus normal in size, anterior, and freely mobile. Both ovaries were slightly enlarged and tender. The right ovary felt cystic. The uterosacral ligaments were thickened and tender.

A provisional diagnosis of pelvic endometriosis was made and androgen therapy instituted. This has yielded uncertain results, to date, after three months of treatment. During this period, the oral afternoon temperatures have ranged between 99.4 and 100° F.

Comment

These five cases seem to confirm the original observation that fever may be a symptom of endometriosis. The mechanism through which the fever is produced is not clear. Certainly, in none of our cases was there enough old blood, either in the peritoneal cavity or in the cystic masses, to explain the rise in temperature. It is possible, however, that tissue reaction, induced by the ectopic endometrium, may produce pyrexia in certain sensitive individuals.

Fever as a symptom of endometriosis has been infrequently and unimpressively mentioned in the extensive literature of this disease. It is not a fre-

quent nor usual symptom, but, in view of our own experience and the reports of Jeffcoate and Holmes, we believe the presence of fever in a patient suspected of having endometriosis should not prejudice the medical attendant against that diagnosis. Pelvic pain and fever do not necessarily mean pelvic inflammatory disease; they may be due to pelvic endometriosis.

References

1. Scott, R. B., and Te Linde, R. W.: *Ann. Surg.* 131: 697, 1950.
2. Keene, F. E., and Kimbrough, R. A., Jr.: *J. A. M. A.* 95: 1164, 1930.
3. Counseller, V. S.: *AM. J. OBST. & GYNEC.* 36: 877, 1938.
4. Counseller, V. S.: *AM. J. OBST. & GYNEC.* 37: 788, 1939.
5. Payne, F. L.: *AM. J. OBST. & GYNEC.* 39: 373, 1940.
6. Fallas, R., and Rosenbloom, G.: *AM. J. OBST. & GYNEC.* 39: 964, 1940.
7. Meigs, J. V.: *Am. J. Surg.* 127: 795, 1948.
8. Holmes, W. R.: *AM. J. OBST. & GYNEC.* 43: 255, 1942.
9. Jeffcoate, T. N. A.: *Obst. & Gynec. Brit. Emp.* 54: 858, 1947.

Discussion

DR. ROBERT KIMBROUGH, JR.—The Society is indebted to Dr. Forman for bringing to our attention that fever is present in a certain number of patients who have endometriosis. Of particular practical value is his point that the presence of fever associated with pelvic masses does not necessarily indicate pelvic inflammatory disease. Certainly there was no inflammatory lesion in the first case cited by Dr. Forman, nor was there evidence of such in the pathologists' reports in Cases 2 and 3. Patient No. 1 has been under my observation since her operation in 1946; unfortunately I have no record of her temperature during this postoperative period. I would like to know whether Dr. Forman can tell us the subsequent temperature pattern in the other two patients who were operated upon. Persistently normal temperatures would strengthen the evidence that active endometriosis may be the cause of fever. If this be true, it is rather difficult to understand why only 8.7 per cent of Holmes' patients, and only 8.8 per cent of Jeffcoate's proved cases presented this symptom.

In this connection it might be interesting to review the work of Reiman, published in 1935, in which he found that 19.77 per cent of the normal ambulatory population might be expected to have temperatures of 99 to 100.4° F. In the following year Reiman published his results of a thorough study of sixteen women who for months or years ran temperatures between 98.6 and 100° F. No cause for the fever could be found in any of the group. Five of the sixteen were considered to be normally adjusted healthy women and the rest were regarded as neurotic. He concluded that a certain proportion of normal individuals have temperatures regulated at levels slightly higher than 98.6° F. and that temperature at these levels is often found in neurotic persons.

Could it not be, therefore, that fever in association with endometriosis is merely coincidental? Might it not be possible that the excitement incident to admission to a hospital accounted for the fever observed in approximately 9 per cent of patients?

Again I would re-emphasize Dr. Forman's excellent point that the presence of fever does not by any means rule out the diagnosis of endometriosis. I have found his presentation profitable and provocative.

DR. FORMAN (Closing).—I quite agree with Dr. Kimbrough that there are definite segments of the population who run temperatures higher than normal but, in this group, two of the three patients who were operated upon definitely had normal temperatures after operation. Cases 1 and 3 were checked for six weeks postoperatively. Case 2 was not carefully checked; however, the impression was that her temperature was normal. The same thing is true of the cases which have been treated medically and in which the diagnosis is unproved. As to what percentage of my own patients with endometriosis have had fever, I would estimate it to be about 15 per cent. In the 12 patients we have studied, from this standpoint, two have shown evidence of fever. Again, I admit this as a clinical observation and I submit it as such. Fever is not a common or striking feature of the disease, but it seemed to me to be of enough clinical significance to report it as another fact in the clinical picture of this interesting disease.

THE EFFECTS OF INTRAVENOUS INJECTIONS OF ERGONOVINE AND METHERGINE ON THE POSTPARTUM PATIENT

J. B. FORMAN, M.D., AND R. L. SULLIVAN, M.D., NEW HAVEN, CONN.

(From the Department of Obstetrics and Gynecology of Yale University School of Medicine)

ERGONOVINE and Pitocin have been investigated with reference to systemic reactions and definite subjective symptoms were found that could be attributed to the administration of these drugs.¹ In addition to such symptoms as flushing, dizziness, headache, tinnitus, perspiration, cramping, etc., there were definite vasopressor actions of both drugs.

After the development of *d* lysergic acid *d* l hydroxybutylamide 2, (Methergine*), in 1943,² many subsequent pharmacological³ and clinical investigations were carried out and proved it to be an effective oxytocic agent.

Many investigators have found that Methergine is effective in reducing blood loss,^{4, 5, 6, 7} while others^{8, 9, 10} found it as satisfactory as ergonovine in this action. A recent report⁴ indicates that if Methergine is used in conjunction with a calcium salt it may even further reduce normal blood loss.

Methergine has been used in the third stage of labor and, in addition to lessening blood loss, it hastened the placental delivery.^{5-7, 9, 11-14} Decreased lochia and hyperinvolution of the uterus^{14, 15} were also reported following administration of Methergine in the postpartum period.

Methergine has also proved itself satisfactory in the induction of labor,^{16, 17} and was shown to be only slightly less effective than Pitocin.

Ergonovine and Methergine have been compared clinically in their ability to contract the uterus and the latter was found to produce stronger contractions of greater duration than ergonovine.^{13, 18, 19} Speed of action was approximately the same; however, when Methergine was used with a calcium salt⁴ there was a further decrease in uterine contraction time.

A recent observer noted that Methergine does not produce as great an elevation of blood pressure as ergonovine.²⁰

Since it was desirable to determine how Methergine compared with ergonovine maleate in relation to systemic effects, the following study was carried out in a manner similar to the investigation of ergonovine and Pitocin.¹

Method

The purpose of this study was to compare the effects of intravenous therapeutic doses of Methergine and ergonovine on the postpartum patient. For the purpose of eliminating inequities due to increased systemic reactions and irritability of the uterus nearer to the day of delivery, the patients were

*The authors wish to thank Sandoz Pharmaceuticals for supplying the Methergine used in this experiment, and Burroughs Wellcome & Co., Inc., for supplying the ergonovine.

divided into two groups of 25 each. In the first group, Series I, the patients received an injection schedule as follows:

- First postpartum day—no oxytocics
- Second postpartum day—1 c.c. (0.2 mg.) ergonovine, intravenously
- Third postpartum day—1 c.c. (0.2 mg.) Methergine, intravenously
- Fourth postpartum day—1 c.c. sterile saline, intravenously

In Series II, the schedule was as follows:

- First postpartum day—no oxytocics
- Second postpartum day—1 c.c. (0.2 mg.) Methergine, intravenously
- Third postpartum day—1 c.c. (0.2 mg.) ergonovine, intravenously
- Fourth postpartum day—1 c.c. sterile saline intravenously

The purpose of saline on the fourth postpartum day in each series was to rule out the possible psychic effect of an intravenous injection. In all cases the drugs were injected over a 30-second period.

The patients were selected with the following considerations in mind: (1) complications of pregnancy; (2) history of hypertension or increased blood pressure above 140 systolic and/or 90 diastolic on admission; (3) duration of labor; (4) type of delivery; (5) blood loss; (6) oxytocics at the end of the third stage.

These considerations were felt to be important in order to have postpartum patients with as near a normal, spontaneous delivery as possible.

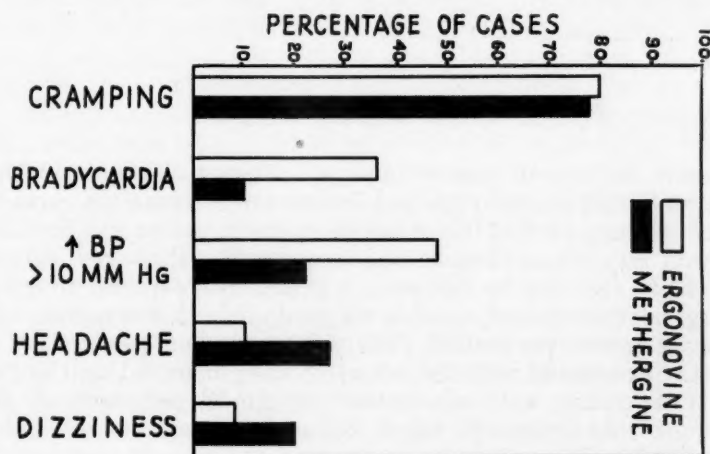


Fig. 1.

The patients in these series all had uncomplicated pregnancies (i.e., no hypertension, excessive weight gain, albuminuria, or edema). The average blood loss of the patients in Series I was 192 c.c. with a range from 50 to 300 c.c. These values were estimated at the time of delivery. In Series II, the average loss was 204 c.c. with a range of 50 to 350 c.c. All deliveries were spontaneous. All patients had blood pressures on admission less than 140 systolic and/or 90 diastolic. The average duration of labor was 8.2 hours in Series I, and 6.6 hours in Series II. The range was from 1 hour, 10 minutes to 17 hours, 46 minutes in Series I. The range in Series II was from 1 hour, 25 minutes to 23 hours. Oxytocics given at the end of the third stage were ergonovine (0.2 mg.), and Pitocin (10 units), intramuscularly. No other oxytocics were given at any time. The purpose of beginning the injections on the second postpartum day in each series was to rule out a possible late effect of oxytocics received at the end of the third stage.

The subjective complaints of the patients in each series were recorded anatomically, and blood pressure recordings were made just prior to the injection of the test drug and one minute following the completion of the injection. A significant blood pressure rise was taken to be 10 mm. of mercury, systolic or diastolic. Rises over 20 mm. of mercury, systolic or diastolic, were also grouped separately. A fall in pulse of 10 beats per minute or more was used to indicate bradycardia. A summary of those signs and symptoms which were significant or showed major differences between the two drugs is outlined in Fig. 1.

In all patients of both series, none could recall any reaction following administration of the oxytocic given at the end of the third stage of labor.

For the purpose of discussion, Series I and II will be combined and reactions to each drug will be the totals of both series. A tabulation of symptoms and signs observed, excluding blood pressure recordings, is seen in Table I.

TABLE I

SYMPTOMS	ERGONOVINE	METHERGINE
<i>Head.</i> —		
(Headache, tinnitus, dizziness, or perspiration)	32%	50%
<i>Thorax.</i> —		
(Chest pain, palpitation, or dyspnea)	4%	12%
<i>Abdomen.</i> —		
(Desire to defecate or to urinate, gas, leg pain, or backache)	28%	16%
Cramping	80%	78%
SIGNS		
Bradycardia	36%	10%
Tachycardia	6%	8%

The most common complaint was cramping. This was observed in 80 per cent of patients receiving ergonovine and 78 per cent of patients receiving Methergine. It was common to find more severe pain in patients injected on the second postpartum day, regardless of the drug used. However, this discomfort could be readily relieved by codeine, 1 grain, and aspirin, 10 grains, in all instances. Ergonovine seemed capable of producing this symptom more frequently in the more recent parturient (100 per cent when injected on the second postpartum day compared with 60 per cent when injected on the third postpartum day). Dieckmann and associates¹ report 57 per cent of their patients complained of this symptom after intravenous ergonovine. Methergine seemed to have the same effect regardless of the time it was injected (76 per cent when injected on the second postpartum day compared with 80 per cent when injected on the third postpartum day). The cramping was coincident with uterine contractions and usually came on within 1 to 2 minutes after the injection of the drug. Symptoms of backache and leg pain were often associated with the cramping and occurred in 16 per cent of those receiving ergonovine and 12 per cent of those receiving Methergine.

The symptoms of headache, tinnitus, perspiration, or dizziness occurred more in patients after Methergine was given than when ergonovine was injected (50 per cent with Methergine compared with 32 per cent with ergonovine). In Dieckmann and his co-workers'¹ series this set of symptoms occurred in 33 per cent of the patients who received ergonovine.

Thoracic symptoms of dyspnea, chest pain, or palpitation were also more frequent with Methergine (12 per cent) than with ergonovine (4 per cent).

Symptoms of flatulence and the desire to urinate were each seen in two patients with ergonovine and in one with Methergine (not the same patients).

Desire to defecate was seen in two patients with ergonovine while no patients receiving Methergine had this sensation. Nausea was seen in three patients each with ergonovine and Methergine (not the same patients). No patients vomited in either group.

Perhaps more significant is the fact that there are vasomotor effects with both drugs, apparently more pronounced with ergonovine. The tabulation of recent reports in Table II shows how ergonovine and/or Methergine affect the blood pressure.

TABLE II

INVESTIGATORS	ERGONOVINE	METHERGINE
Dieckmann, et al. ¹ (Increase greater than 10 mm. Hg)	58%	--
Schade ²⁰ (Increase greater than 20 mm. Hg)	31.6%	11.3%
Sandin and Hardy ⁴ (Increase greater than 10 mm. Hg)	--	20%
In the present series:		
Increase greater than 10 mm. Hg	48%	22%
Increase greater than 20 mm. Hg	22%	10%

Forty-eight per cent of the patients receiving ergonovine had a rise in blood pressure over 10 mm. of mercury, systolic or diastolic, compared with 22 per cent with Methergine. If 20 mm. of mercury, systolic or diastolic, is used as a significant rise in blood pressure, the relationship is 22 per cent with ergonovine and 10 per cent with Methergine. It was observed that when the increase in blood pressure was over 20 mm. of mercury, the rise was usually in the systolic pressure with ergonovine (10 cases in 11). However, with Methergine, no relationship could be seen, for in 5 cases 5 had the rise in the systolic pressure and 4 had the rise in the diastolic pressure. If the measure of elevation was 10 mm. of mercury or greater, the rise with ergonovine in the systolic pressure decreased in frequency ratio to the rise in the diastolic (20 and 14 cases for ergonovine; 9 and 8 cases with Methergine).

No other relationship could be seen between systolic or diastolic pressures with the two drugs. It was evident, however, that the more recent parturient has greater blood pressure changes. When injected on the second postpartum day, ergonovine produced an elevation greater than 10 mm. of mercury in 64 per cent of the patients and in only 32 per cent when given on the third postpartum day. Methergine did not show variation to this degree. It produced rises greater than 10 mm. of mercury in 24 per cent when given on the second postpartum day compared with 20 per cent on the third postpartum day.

Bradycardia was seen in 36 per cent of the patients receiving ergonovine and in 10 per cent of the patients receiving Methergine.

Only two patients experienced any symptoms following administration of saline intravenously. One of these experienced dizziness. She had previously felt this same symptom with the test drugs. The other patient had a "cold feeling" over her body. This had not been experienced after the test drugs. In no case was there a rise in the blood pressure above 10 mm. of mercury following saline administration.

Summary

There were definite symptoms and signs associated with the intravenous administration of ergonovine and Methergine in 50 postpartum patients. The subjective symptoms in postpartum patients receiving either ergonovine or Methergine were transient and variable, but potentially distressing to the patients. Very few of these symptoms can be attributed to the psychic effect of an intravenous injection.

Abdominal symptoms of cramping are the most common and were about equal with the two drugs (80 per cent and 78 per cent with ergonovine and Methergine, respectively).

Cerebral symptoms of headache, tinnitus, dizziness, or perspiration are more common with Methergine (50 per cent) than with ergonovine (32 per cent).

Thoracic symptoms of chest pain, palpitation, or dyspnea were also more common with Methergine (12 per cent) than with ergonovine (4 per cent), although the number of cases having these complaints is small.

Comparisons of results in the present series with those in other series in Table II can be made although the drugs were given at a later time than in either Schade's or Sandin and Hardy's series. It is generally accepted that the more recent parturient reacts to oxytocics more strongly quantitatively than patients farther past their delivery date. In Dieckmann, Forman, and Phillips' series they injected 2 c.c. (0.4 mg.) of ergonovine which is twice the dose used in the present series. In any case, ergonovine seems to have a greater vasopressor action as one of its systemic reactions than Methergine. For this series 48 per cent and 22 per cent of patients receiving ergonovine had a rise in blood pressure greater than 10 mm. or 20 mm. of mercury, respectively. This can be compared with rises of 22 per cent and 10 per cent for Methergine under the same conditions.

Ergonovine is more pronounced than Methergine in vasopressor effect on postpartum patients and it is suggested that perhaps the latter drug would be more desirable if patients already had elevated blood pressure.

Bradycardia was seen in 36 per cent of the patients receiving ergonovine and in 10 per cent of the patients after Methergine was given. It is possible that these systemic reactions of vasopressor action and bradycardia could, in certain cases, mask symptoms of impending shock in the postpartum patient.

References

1. Dieckmann, W. J., Forman, J. B., and Phillips, G. W.: *AM. J. OBST. & GYNEC.* 60: 655, 1950.
2. Stoll, A., and Hoffman, A.: U. S. Patents Nos. 2,265,207 and 2,265,217.
3. Kirchhoff, A. C., Racely, C. A., Wilson, W. M., and David, N. A.: *West. J. Surg.* 52: 197, 1944.
4. Sandin, H. V., and Hardy, J. A.: *AM. J. OBST. & GYNEC.* 61: 1087, 1951.
5. Baskin, M. J., Harvey, E. L., and McEndaffer, D. M.: *Rocky Mountain M. J.* 44: 208, 1947.
6. Bunch, J. R.: *Rocky Mountain M. J.* 45: 1110, 1948.
7. Tritsch, J. E., Schneider, E., and Longworth, E. F.: *New York State J. Med.* 48: 293, 1948.
8. Schade, F. F., and Gernand, H. C.: *AM. J. OBST. & GYNEC.* 59: 627, 1950.
9. Williams, B. C.: *Rocky Mountain M. J.* 44: 207, 1947.
10. Riordan, L. M., Stricker, H. C., Correnti, N. A., and Torkelson, H. P.: *J. Missouri M. A.* 47: 108, 1950.
11. Tritsch, J. E., and Schneider, E.: *AM. J. OBST. & GYNEC.* 50: 434, 1945.
12. Hepp, L. C., and Evans, J. R.: *Rocky Mountain M. J.* 42: 949, 1945.
13. Roberts, P. C.: *West. J. Surg.* 52: 380, 1944.
14. Gipstein, B. L.: *AM. J. OBST. & GYNEC.* 54: 1065, 1947.
15. Pannullo, J. N.: *J. M. Soc. New Jersey* 45: 523, 1948.
16. Brougher, J. C.: *West. J. Surg.* 55: 371, 1947.
17. Farber, E. P.: *Clin. Med.* 55: 37, 1948.
18. Cartwright, E. W., and Rogers, W. C.: *West. J. Surg.* 54: 59, 1946.
19. Gill, R. C.: *J. Obst. & Gynaec. Brit. Emp.* 54: 482, 1947.
20. Schade, F. F.: *AM. J. OBST. & GYNEC.* 61: 188, 1951.

EVALUATION OF CERVICAL BIOPSY IN THE DIAGNOSIS OF CARCINOMA*

CLAYTON T. BEECHAM, M.D., AND JOHN EMICH, M.D., PHILADELPHIA, PA.

(From the Department of Obstetrics and Gynecology, Temple University Medical School and Hospital)

CANCER detection is assuming a major role in medical practice today as more and more patients are coming to their physicians for periodic physical examinations. In this direction a noteworthy advance in cancer detection has centered in the cytologic screening method introduced by Papanicolaou. Welcome as this new aid has been, it has given rise to additional problems. It has been pointed out repeatedly that the cost and the lack of personnel constitute the chief deterrents to a more widespread employment of this diagnostic method. The Obstetric and Gynecologic staff at Temple University School of Medicine find themselves in the same position as many others regarding these two factors. If vaginal smears were to be used by us as a method of early detection of cervical malignancy, a tremendous cytologic effort would be required, for in addition to the private patients of a fourteen-man staff, approximately 19,000 clinic patients are examined each year.

Recently Novak¹ has summed up our position as follows: "The present status of the question (vaginal smears) is still that the method is of distinct value as a screening process in the hands of trained cytologists, that the latter are still lamentably few in number, that there are a good many pitfalls in the interpretation of vaginal smears, that cytologic diagnosis in itself is not decisive and should not be made the basis for treatment, and that the routine employment of the method is time-consuming and expensive.

"Useful as such cytologic studies have been in well-equipped clinics, one cannot feel sure that thus far they have made any notable impression on cancer mortality in general. At the risk of being labeled a reactionary, it is my honest opinion that more lives could be saved by pushing education of both the laity and the profession in the life-saving possibilities of periodic examinations at intervals of every six months, regardless of whether or not there are symptoms of any kind."

In our institution we must screen and diagnose our cancer cases by employing the standard everyday procedures of medical practice, namely, a complete history and physical examination and free use of the biopsy, while maintaining at all times a high degree of suspicion regarding cancer. We have been concerned over the employment of only these bare essentials of diagnostic medicine and our failure to employ vaginal cytology has caused us to question seriously our work to date. Since cervical carcinoma is the most common malignant lesion in the female, we have studied this one anatomical area for an appraisal of our success.

*Presented at a meeting of the Philadelphia Obstetrical Society, Oct. 4, 1951.

Material

We have done 2,145 cervical biopsies in a period of 68 months, from Jan. 1, 1946, to Sept. 1, 1951. Cervicitis in its various forms was diagnosed 2,017 times. Invasive carcinoma was found in 107 cases and noninvasive carcinoma in 21 instances, for a total of 128 cases of cervical malignancy (Table I).

To evaluate this method of *suspicion and biopsy* one must disregard those cases wherein the diagnosis of carcinoma was obvious. Since we view every cervix with suspicion one must rightly ask how we choose the cases for biopsy where there is no evidence of malignancy. The following criteria are used as guides by us: first, the lesion that demonstrates the slightest bleeding on sponging with cotton, at any age level; second, all cervical lesions in women over 35 years of age before treatment is instituted; third, all cervical lesions that arouse suspicion in the examiner's mind even though there are no signs of traumatic bleeding. Unsatisfactory as these criteria may appear we have discovered 28.0 per cent of our total by this means. Cervical specimens were obtained by the use of the punch biopsy. The sites of elective biopsy were quadrant in type, at 12, 3, 6, and 9 "o'clock." In those cases which demonstrate a suspicious lesion, the lesion was biopsied. In either instance the tissues obtained were placed in separate vials labeled with the site of origin.

TABLE I. CERVICAL BIOPSIES, 5½ YEARS—2,145 BIOPSIES

	NO.	PER CENT
Cervicitis, various forms	2,017	94.0
Benign lesions		
Carcinoma 107	128	6.0
Noninvasive carcinoma 21		

Three of our 21 cases of carcinoma in situ cannot be included in our early diagnostic group, since they were massive lesions and grossly appeared to be invasive cancer. Further biopsy and operative specimen proved the "non-invasive" diagnosis to be correct (Tables II and III).

TABLE II. INVASIVE CARCINOMA OF THE CERVIX

	NO.	PER CENT
Invasive carcinoma	107	83.5
Invasive carcinoma (107) not evident on gross examination	18	14.0

TABLE III. NONINVASIVE CARCINOMA

	NO.	PER CENT
Noninvasive carcinoma	21	16.4
Invasive carcinoma suspected on gross examination	3	2.3
<i>Summary.</i> —		
Invasive and noninvasive carcinoma diagnosed but not evident on examination	36	28

The next questions to be answered in appraising this work are whether we have missed cases of cervical cancer in our examinations and if so when was the diagnosis established and by whom. For the answers we have turned to the "Committee for the Study of Pelvic Cancer" in Philadelphia. This committee has been investigating pelvic malignancy for the past seven years and

since we have used only the material of the past five years and eight months we believe that our errors should be in evidence by this time. Thus far no one of our staff has been responsible for a delay in diagnosis of cervical carcinoma as shown by the investigations of this committee.

Summary

1. History, physical examination, free use of the biopsy, and maintainance of a high index of suspicion have been rewarding in the diagnosis of early cervical carcinoma.

2. Twenty-eight per cent of our cases of carcinoma of the cervix were not clinically evident and were diagnosed by suspicion and biopsy.

3. Resident and teaching staffs caring for private and ward patients have thus far not been responsible for delay in the diagnosis of cervical carcinoma.

Our sincere thanks to Mr. Fred Curtis for assisting in the collection of data.

Reference

1. Novak, E.: *Obst. & Gynec. Surv.* 5: 880, 1950.

Discussion

DR. T. M. MONTGOMERY.—From conference with Dr. Beecham I take it that in this paper he is endeavoring to point out that good gynecology can be practiced without the help of Papanicolaou smears. His results would indicate that an alert specialist and a well-conducted clinic can, by the use of the tried and proved methods of inspection, palpation, curettage, and biopsy, demonstrate the presence of clinically significant cancer of the uterus in time for adequate therapy. This observation should be of comfort to those gynecologists to whom the facilities of a cytological laboratory are not yet available.

I think Dr. Beecham asked me to discuss his paper because at one time in conversation I stated that thus far in the number of smears that I have collected in private practice (1,895 from 1946 to date) I had not yet encountered a case of cancer in which the diagnosis had not also been indicated by parallel observations. I have hesitated to make this statement in public, realizing that the preponderance of evidence from reports in the literature has been otherwise, and feeling that my own contradictory observations might have been due to slight differences in technique, or coincidence, or different patient material, or more conservative interpretation on the part of the laboratory to which I send my slides. Nevertheless, such has been my experience and to that degree it would seem to confirm what Dr. Beecham has stated.

However, the chance experience of a gynecologist here, or even of an active clinic, does not detract from the over-all value of cytological studies as a screening test for uterine cancer. I would not give up the Papanicolaou smear or its modifications, and doubtless Dr. Beecham would desire to have the facilities of a cytological laboratory if they were readily available.

The development of screening methods for pelvic cancer, and the investigation of readier procedures for early diagnosis must go on, for, while inspection, curettage, and surgical biopsy may satisfy the requirements of the specialist in the case of referred patients, they are by no means satisfying the need for early diagnosis in the population at large.

In the latter respect one has only to review the problems of the general practitioner as presented before the Pelvic Cancer Committee of Philadelphia. The Committee has been urging him to examine all of his patients pelvically and thus detect cancer at an early stage. In general he replies as follows:

"You exhort us to make a pelvic examination to recognize early cancer but you offer no practical procedure by which we can fix a diagnosis. Papanicolaou smears are not generally available to us. Office biopsy is a bit difficult and produces embarrassing degrees of bleeding.

Our patients do not want to run to a clinic or a specialist's office for every local complaint and every erosion of the cervix. Give us a safe, reasonably sure procedure to screen these patients in our office."

Thus far there has been no satisfactory answer to this request, although it presents the present crux of the situation. Many feel that the providing of widespread availability of Papanicolaou smears is not the answer because of expense, lack of trained personnel, and the fallibility of the procedure itself. Perhaps the possibilities of sponge biopsy, cervical scrapings, etc., have not been fully explored, or in some combination of all of these the answer may be found. In the meantime, we are correct in urging the practitioner to feel and look, as the best basis for present preliminary diagnosis; and in depending upon curettage and biopsy for final proof.

DR. LEWIS C. SCHEFFEY.—I am sorry that Dr. Howson was not here to speak because we all have confidence in his judgment, and in the experience he has obtained from conducting the monthly meetings of the Committee for the Study of Pelvic Cancer with the finesse that is his. First of all, I would like to congratulate Dr. Beecham and Dr. Emich for the presentation of a careful and thorough piece of work. I think that we could not help but be impressed by the statistics that he showed; second, and probably of decided importance in the eyes of many, the fact that there were no late cases in which his hospital was involved. That is a record that they can well be very proud of. With respect to the problem at hand, I am afraid too often that we, as specialists, talk and act as though everyone who has an opportunity to detect cancer early has our facilities. However, this is a specialists' meeting and we are talking of work as done by specialists. As to the Papanicolaou smear, I doubt if there is a man in the room who does not agree with Dr. Beecham, that it cannot replace meticulous examination and a carefully studied biopsy. Dr. Montgomery said that he had obtained no positive information from the Papanicolaou smear in 1,895 examinations, but that he would hesitate, nevertheless, to give up its use. Certainly, reports in the literature show its value even in the presence of minimal cervical lesions. The Philadelphia Division of the American Cancer Society decided to give up the Papanicolaou smear service in the local Detection Clinics because the cost did not show enough positive figures to justify the expense. However, there we are dealing with supposedly well people. We should approach this whole question of cervical cancer detection from all of the angles that have been presented. By all means use Papanicolaou smears if you have the opportunity. The cervix that appears grossly normal may yield a suspicious or even a positive report. Certainly, taking a "spot biopsy" is an excellent thing to do when you are confronted with an obviously localized abnormality of the cervix; but there is something else to think about. Everyone in this room deals with abnormal and diseased cervixes. Because of this, we have not only the opportunity but the obligation to correct such conditions, by amputation of the cervix as a surgical procedure when combined with other operative measures or by circular biopsy followed by endothermic desiccation. Our feeling is that it is important to remove enough tissue thereby to give the pathologist a collar of uncharred tissue for serial study. You will thus be performing two services—possibly making an early cancer diagnosis, and putting the cervix in good condition for the future. I would like to show several slides to illustrate some of the things of which I have spoken, but I do not want to go into the controversial question of carcinoma in situ at this time because I am still "up in the air about it," as I suppose many others are—especially in view of the variety of opinions expressed by pathologists regarding the different aspects of this very pertinent problem.

DR. GLENN S. DICKSON.—It has been brought out that in many cases apparently normal cervixes have been found to have invasive carcinoma. If that is true, should Papanicolaou smears be done in all cases coming to us for gynecologic examination?

DR. ROBERT M. HUNTER.—I, like the essayist, feel that there is no substitute for a good history and careful bimanual and speculum examination. I am especially interested in those cases that had a positive biopsy for invasive carcinoma yet were not suspected of malignancy clinically.

DR. JOHN B. MONTGOMERY.—Six per cent of positive biopsies is rather high. I realize that these biopsies were made only on diseased cervixes; however, unless the group included patients referred with gross cancer, the finding of .6 per cent of carcinomas in routine biopsies impresses me as very high.

DR. BEECHAM (Closing).—Dr. Hunter asked about the indications for biopsy and whether it was a routine procedure. In the text of the paper we outlined our criteria for biopsy since it would have been an impossible task to biopsy every cervix visualized in clinic. I believe this accounts for the relatively high incidence of malignancy as questioned by Dr. John Montgomery, for these were grossly diseased cervixes. Dr. Hoffman questioned the diagnosis of preinvasive carcinoma. In answer to this, we have included it in the list of diagnoses because in three cases it appeared grossly as an invasive carcinoma. I may add that our understanding of this pathologic entity leaves much to be desired.

Formerly, we used the circular biopsy obtained by the "cold knife" as advocated by Dr. Scheffy but there were several undesirable features with this method. First, the pathologists were not obtaining enough sections from the tissue; second, they had no idea of where the suspicious lesion was located; third, when a questionable area was discovered by pathologists we had no way of orienting ourselves as to the area of suspicion; and, last, this is a procedure which should be done in the operating room and not in the office. Since the timely paper of Foote and Stewart we have used the quadrant type of biopsy as noted in the paper.

MISSED ABORTION—A STUDY WITH THE TOKODYNAMOMETER*

GILLIAN ROWE-DUTTON, M.B. (OXON),** OXFORD, ENGLAND, SAMUEL LUBIN, M.D., BROOKLYN, N. Y., SAMUEL R. M. REYNOLDS, PH.D., D.SC., BALTIMORE, MD., AND RICHARD WALTMAN, M.D., BROOKLYN, N. Y.

(From the Department of Obstetrics and Gynecology, State University of New York, College of Medicine, Cumberland Hospital, Brooklyn, N. Y., and the Department of Embryology, Carnegie Institute of Washington, Baltimore, Md.)

MISSED abortion, an obstetric complication resulting from abnormal retention of dead products of conception, is a relatively disturbing physical and psychological condition for the patient as well as for her obstetrician. While we may perhaps encounter this entity with increasing frequency because of the large doses of estrogen being employed in cases of threatened abortion, the means of emptying the uterus are by no means completely agreed upon. Many advocate priming of the uterus with large doses of estrogen to be followed by Pituitrin injections,¹ while others advise surgical evacuation of the uterus as soon as diagnosis is made or if hormone induction of labor fails.^{2, 3, 4}

In previous publications,^{5, 6} we have advised a conservative policy of watchful waiting for spontaneous expulsion of the retained products of conception, but have felt that hormone induction of labor with estrogen and Pituitrin was relatively innocuous. Surgical evacuation of the uterus, with the attending cervical laceration, uterine atony, hemorrhage, and perforation, was not recommended. Recently we had the opportunity of studying the uterine motility in one patient in this condition with the multichannel tokodynamometer. We present the findings as follows:

A. M., Case 173052, 44 years of age, gravida viii, para vi, with one spontaneous abortion at two months, was admitted to Cumberland Hospital on Feb. 20, 1951, because of pre-eclampsia. Her menses were regular, beginning at age 14, recurring every 28 days, and lasting for 6 days. The last menstrual period was Aug. 31, 1950, and the expected date of confinement was June 7, 1951. On admission, the blood pressure was 186-190/124-130, the extremities showed one plus edema, while urinalysis was essentially normal. The uterine fundus reached to the umbilicus and the fetal heartbeat was in the left lower quadrant, regular at 148. Blood chemistry values were normal, the Wassermann test negative, and the Rh factor positive. An x-ray of the chest revealed no abnormal findings. The patient was placed on a salt-free diet, including hypertonic glucose intravenously and magnesium sulfate orally. She responded with a fall of blood pressure to 140/100. This was her original tension in the clinic in the early months of gestation at which time she had a diagnosis of essential hypertension. She was followed in the prenatal clinic and her second hospital admission was from March 20, 1951, to April 21, 1951.

This time she was admitted because of lack of growth of the fundus, absence of fetal heart sounds, absent fetal movements and weight loss. The blood pressure was 170/130, the urine showed 3 to 4 plus proteinuria and the lower extremities showed a 2 plus edema.

*Aided by a grant from The Kate Lubin Research Foundation, Inc.

**Research Fellow.

The fundus reached the umbilicus and measured 18 cm., which was less than on Feb. 13, 1951. The cervix on rectal examination was long and closed. The blood pressure fell gradually, finally reached 118/80 and the urine became protein free on April 2, 1951.

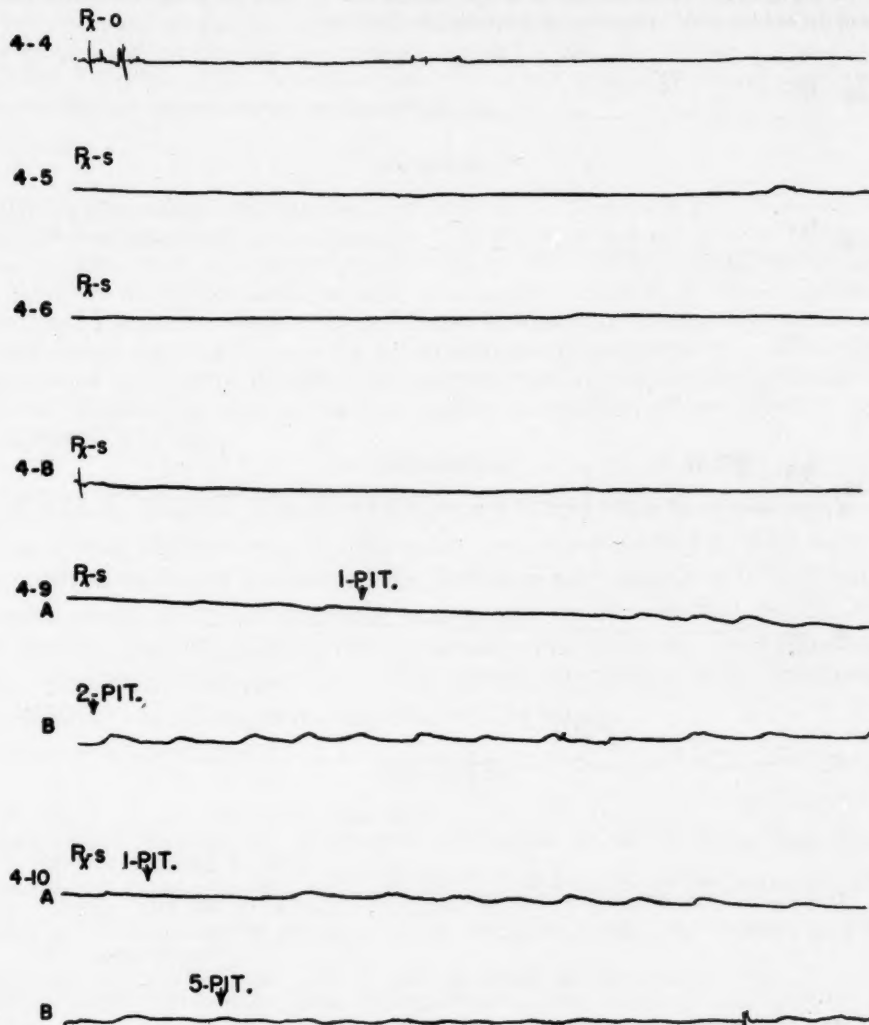


Fig. 1.—Rx-O—No medication
Rx-S—Oral stilbestrol
1-Pit.—First Pitocin injection subcutaneously
2-Pit.—Second Pitocin series subcutaneously
5-Pit.—Fifth Pitocin injection
Pit. iv.—Pitocin intravenously
Dem.—Demerol intravenously

When the patient was stabilized, daily tokodynamometer tracings were begun. On April 5, 1951, oral stilbestrol in doses of 200 mg. three times a day was begun and given for the next five days, inclusive, with a total dosage of 3,000 mg. After this period, 75 mg. were given daily orally from April 10, 1951, through April 16, 1951. Tokodynamometer tracings were taken beginning April 4, 1951, and repeated daily while stilbestrol was administered. To study the effect of Pitocin on an estrogen-primed uterus, on April 9, 1951, Pitocin, 0.2 c.c. given every thirty minutes subcutaneously for five doses, was exhibited. On April 10, 1951, the following day, Pitocin dosages of 0.25 c.c., 0.5 c.c., and

then 1 c.c. for three doses were administered subcutaneously. On April 11, 1951, no oxytocic was administered. On April 12, 1951, posterior pituitary solution in doses of 2 minims subcutaneously administered at thirty-minute intervals for four doses was employed. During these trials, blood pressure recordings showed no rise. On April 14, 1951, there was no evidence of spontaneous uterine contractions.

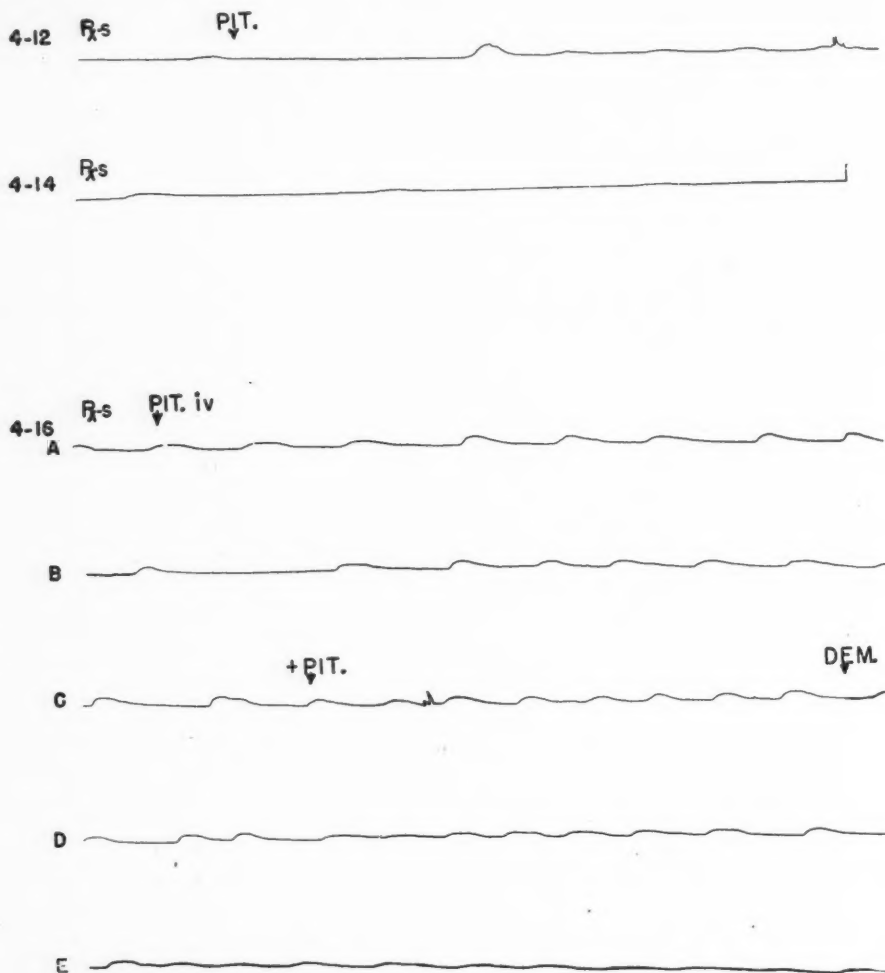


Fig. 2.—Rx-O—No medication
 Rx-S—Oral stilbestrol
 1-Pit.—First Pitocin injection subcutaneously
 2-Pit.—Second Pitocin series subcutaneously
 5-Pit.—Fifth Pitocin injection
 Pit. iv—Pitocin intravenously
 Dem.—Demerol intravenously

Two days later, on April 16, 1951, intravenous Pituitrin therapy in dilution of 1:5,000 was begun, the first 500 c.c. at the rate of 25 drops per minute and the next 400 c.c. at 50 drops per minute. During the course of this administration, uterine contractions were effectual and 100 mg. of Demerol were given slowly by vein. After a total of four hours, the patient delivered spontaneously a macerated stillborn male infant from left sacro-anterior position with placenta and membranes complete. There was minimal blood loss.

The placenta was covered with multiple infarcts and the microscopic examination showed inter- and intravillous fibrosis with areas of calcification. During the course of

stilbestrol administration, the consistency of the cervix was followed by repeated rectal examinations and the long thick parous cervix remained unchanged. Two x-ray examinations of the abdomen revealed overriding of the fetal skull bones and overriding of the sutures, indicative of fetal death. A kidney function test showed diluting power to 1.004 and concentrating power up to 1.026. Blood chemistry tests were repeatedly normal. Blood hemoglobin, on the second admission, March 21, 1951, was 80 per cent and red blood cells were 4,200,000. Five days after delivery of the fetus, the patient was discharged in good condition with a blood pressure of 118/80.

Summary

No spontaneous uterine contractions were observed in a case of missed abortion that received no medication. Likewise, after priming with large oral doses of stilbestrol, no contractions were noted. Three unsuccessful trials to induce labor on different days with increasing dosages of subcutaneously administered Pituitrin resulted in mild and ineffectual uterine contractions. On the following day, there was no spontaneous uterine activity. With the continuation of stilbestrol medication, intravenous Pituitrin drip associated with Demerol resulted in spontaneous complete evacuation of the uterine contents and minimal bleeding.

Conclusion

It is quite possible that the same results would have been obtained without the use of the above therapy. We must remember, however, that many cases of missed abortion, as mentioned by Jeffcoate and ourselves in previous publications, went on to spontaneous evacuation when admitted to the hospital with bleeding and/or pain. From the findings in this case, there appears to be some correlation between the oral stilbestrol, intravenous Pituitrin and Demerol, and the subsequent evacuation of the uterus.

References

1. Jeffcoate, T. N. A.: *Lancet* 1: 1045, 1940.
2. Titus, Paul: *Management of Obstetric Difficulties*, ed. 2, St. Louis, 1940, The C. V. Mosby Company, p. 295.
3. Greenhill, J. P., and De Lee, J. B.: *Principles and Practice of Obstetrics*, ed. 10, Philadelphia, 1951, W. B. Saunders Company, p. 408.
4. Beck, A. C.: *Obstetrical Practice*, ed. 3, Baltimore, 1942, The Williams and Wilkins Company, p. 507.
5. Lubin, S., and Waltman, R.: *AM. J. OBST. & GYNEC.* 45: 89, 1943.
6. Lubin, S., and Waltman, R.: *Am. J. Surg.* 77: 202, 1949.

CULDOSCOPY*

ALBERT DECKER, M.D., NEW YORK, N. Y.

A GYNECOLOGIST is usually able to palpate most pathological conditions in the pelvis with an exactness that requires little or no presumption. A number of conditions that are palpably indefinite permit a strongly presumptive diagnosis when correlated with detailed clinical history.

Discovery of a method to determine tubal patency and motility, the perfection of uterosalpingography, and the development of fairly accurate methods to determine the functional activity of the organs of reproduction have greatly increased diagnostic ability. However, there still appears an occasional case that is difficult or impossible to diagnose accurately. The urgency of the situation is understandable when it is realized that laparotomy may be demanded or denied according to the accuracy of preliminary diagnosis. These occasional obscure pelvic conditions have been the incentive for the introduction and development during the past fifty years of methods of visual diagnosis by means of optical telescopes introduced into the peritoneal cavity. This procedure has been known by various names in various places during the years of its development.

The pioneers preferred the designations "celoscopy" and "laparoscopy," but later workers have popularized the term "peritoneoscopy." In recent years, however, the terms "celioscopy" and "splachnoscopia" have appeared in medical dictionaries.

Notwithstanding the fact that peritoneoscopy is comparatively harmless and has been usefully employed in disclosing obscure pathological processes in the pelvis, it has been little used in gynecologic practice.

In an attempt to improve the usefulness of celioscopy in gynecology, a new technique has been introduced that varies in many respects from that previously employed. This method, termed "culdoscopy," is a procedure of visualization of the pelvic organs by means of a telescopic optical instrument passed through the punctured posterior fornix while the patient is in the knee-chest position. There are many advantages to this method, which appears to be a satisfactory solution of celioscopy in women and a valuable adjunct to the gynecologic diagnostic armamentarium.

It was the choice of the knee-chest position that made possible the development of the technique of culdoscopy. When the pelvis is elevated above the hips and the abdomen is relaxed and dependent, the abdominal and pelvic viscera change their positions and are displaced cephalad. The result is increased intra-abdominal pressure under the diaphragm and decreased or nega-

*Read at a meeting of the New York Obstetrical Society, Oct. 9, 1951.

tive pressure in the pelvis. Under these conditions, when the vaginal introitus is opened, the vagina distends and the mucous membrane becomes stretched and thinned out, losing its rugate appearance. The pressure within the stomach and upper bowel is increased, while the pressure in the rectum and sigmoid is diminished, tending to collapse these organs. The distended vagina separates the rectum from the cervix by several centimeters. This establishes a proximity between the vaginal mucous membrane and the peritoneum of the cul-de-sac. When the intervening extraperitoneal fatty tissue is present as a very thin layer, the approximation of these structures results in a very thin vaginal septum.

When the vaginal septum is taut and thinned out, it may be readily punctured with a trocar of considerable size with very little discomfort to the patient. The knee-chest position causes the intestines to move out of the pelvis so that they escape trauma at the time of puncture and do not obscure the field of vision during telescopic visualization. There can be no compromise with the position. Knee-elbow, knee-head, or squatting positions do not allow relaxation of the abdominal muscles that diminishes intrapelvic pressure and distends the vaginal vault for puncture.

Any consideration of culdoscopy poses two obvious questions:

1. Can puncture be safely performed by a simple technique that is easily acquired?
2. Can the telescopic findings provide adequate data for a conclusion in a large group of cases presenting diagnostic problems?

The knee-chest technique for cul-de-sac puncture, using needles and trocars of various sizes, has now been employed more than 1,500 times as a procedure in office, clinic, ward, and operating room. The findings and results are the bases for these remarks.

Many surgeons with extensive experience in the treatment of endometriosis and tubal pregnancy have been hesitant to puncture the posterior fornix when these conditions were suspected. We have had no unfavorable consequences in doing so, however.

As mentioned elsewhere, culdoscopy is not employed to confirm the obvious. A large fixed mass in the cul-de-sac will not permit complete puncture. Ruptured tubal pregnancy, presenting a typical history with shock and crepitant bulging cul-de-sac, does not usually require puncture for confirmation. Fixation of the rectum or sigmoid to the posterior surface of the uterus, cervix, or vagina is nearly always discernible by palpation. Such immobilization of the posterior fornix is immediately disclosed when the vagina is inspected in the knee-chest position. Distention and stretching of the vaginal vault, usually produced by posture, do not occur in these conditions, and puncture is not attempted.

On the other hand, an apparently fixed, retrodisplaced uterus may move forward sufficiently, while the patient is in the knee-chest position, to permit herniation of the vaginal vault behind it, through which the pelvis may be entered by trocar for successful culdoscopic examination.

When inspection of the vaginal vault in knee-chest position reveals characteristic distention and stretching of the posterior septum, not distorted by manipulation of the cervix, puncture may be safely performed in the presence of extensive pelvic pathology.

When the technique we have described is followed carefully, in properly selected cases, untoward results of puncture need not be anticipated. Using only a local anesthetic wheal, the taut-stretched septum permits puncture with one thrust of a large trocar.

This brings us to the second question: Can the telescopic findings provide adequate data for a conclusion in a large group of cases presenting diagnostic problems?

In most conditions in which gross visual diagnosis is possible, sufficient information may be obtained to permit of a diagnosis. The situation must be such that visualization alone, or with limited displacement and manipulation of the organs, will reveal the pathological process with considerable accuracy. Some experience is required, however, to interpret correctly all the telescopic pictures encountered.

When the normal pelvis, with normal uterus, tubes, and ovaries, is revealed, complete detailed observation is nearly always possible, including many physiological changes in these organs.

The location, size, and color of small ovarian cysts and pelvic tumors are discernible. Peritoneal or intestinal tuberculosis, blood clots, adhesions, distorted fixed fimbriae, adherent fixed tubes, tubal rupture, and the blebs, cysts, and scars of endometriosis have all been observed, each unmistakable in appearance and identity. During examination, it is possible to aspirate free or encysted fluid material from the pelvis, and, when the pathology is favorably located, to remove small amounts of tissue for biopsy.

Pelvic endometriosis in various sites has been diagnosed by culdoscopy in 48 cases. In 20 of these, it was an unsuspected finding during examinations conducted for other purposes.

In some instances of unexplained sterility, it has been possible to determine the exact condition of the uterus, tubes, fimbriae, and ovaries. These determinations have occasionally been helpful in the choice of further therapy. Observations have been made while the tubes were being insufflated by the Rubin technique, but with pressure up to 350 mm. of mercury, and tubal release has been accomplished by the high pressure and manipulation, when insufflation alone had failed.

Culdoscopy has been employed 46 times in 55 cases, in which atypical tubal pregnancy was seriously considered or in which unsuspected tubal pregnancy was disclosed. In these instances, one or several procedures were used (examination under anesthesia, dilatation and curettage, cul-de-sac aspiration, culdoscopy, and surgical exploration).

The diagnosis of tubal pregnancy was made in 24 cases, and confirmed in 19. Of the 19 proved instances, diagnosis was made by puncture and culdos-

copy in 14, by observation and expectancy in 2, and by surgical exploration in 3. In the 5 cases erroneously diagnosed, surgical exploration accounted for 4, and culdoscopy for only one.

In 31 instances, tubal pregnancy was excluded by culdoscopy usually after only several days of observation. The information gained permitted earlier termination of hospitalization or institution of proper therapy for each patient.

We have found that intelligent expectancy, together with the diagnostic procedure of cul-de-sac puncture and culdoscopy, has increased the rate of correct diagnosis in cases of tubal pregnancy with atypical history and physical signs; has shortened the period of hospital observation for cases in which a diagnosis of tubal pregnancy was involved; and has led to the institution of proper therapy in each instance.

Our experience with this procedure appears to warrant these conclusions:

Cul-de-sac puncture in the knee-chest position is a safe procedure, less painful than others, the technique simple and readily acquired. It may be completed in a few moments and need not require operating room facilities.

It is frequently possible for an experienced culdoscopist to puncture the cul-de-sac with a trocar, using only local anesthesia, and to make a visual culdoscopic diagnosis of obscure pelvic conditions.

Successful puncture and telescopic examination were possible in 98 per cent of examinations attempted.

When puncture is readily made and complete examination is possible, the information gained is usually invaluable.

When puncture is unsuccessful, or visual diagnosis is impossible or incomplete, it is at least without great inconvenience to either patient or surgeon.

10 WEST 74TH STREET

Discussion

DR. CHARLES L. BUXTON.—Since 1947, we have done 91 culdoscopies at Sloane Hospital and have found it to be an extremely useful adjunct in making a diagnosis. In fact, in all the cases of the type which Dr. Decker mentioned, we found this procedure to be valuable as an aid for diagnosis.

I have been especially interested in it in connection with diagnosing various different kinds of sterility and endocrine problems, especially in connection with different types of abnormal ovarian function, for instance, the Stein-Leventhal syndrome, etc.

An individual with amenorrhea and ovarian enlargement by pelvic examination is a very good subject for this type of examination because it is possible to visualize accurately the ovaries and thus determine actually a lot about their pathology before deciding on the necessity of a laparotomy.

I think, of course, that everybody wonders whether or not this might be a dangerous procedure, whether it might possibly produce hemorrhage, or bowel perforation, or infection. Of the 91 cases which have been done at Sloane, I know of only two complications. One was in an individual who was admitted to another hospital, about a week after culdoscopy, with a mass in the posterior fornix, which upon examination ruptured and about 200 or 300 c.c. of encysted blood were evacuated. The patient was kept in the hospital for observation for about two days and then sent home.

One other patient, who was examined at Sloane, developed considerable air distention between the leaves of the mesentery of the sigmoid which was incidentally noticed

at subsequent operation, done because the patient had fibroids. This air was observed but I do not believe it would have been of any particular eventual danger. It was considered as a complication, however.

I would like to ask Dr. Decker if he no longer uses carbon dioxide to fill the peritoneal cavity or whether he has now given that up and considers air instead as being perfectly satisfactory.

DR. LOUIS M. HELLMAN.—Dr. Decker, as usual, has been exceedingly modest in discussing what I think is a very significant contribution to pelvic diagnosis. Prior to the advent of this technique, I had considerable experience with the peritoneoscope. The use of that instrument was fraught with danger to the patient. However, with the advent of the culdoscope, used in the knee-chest position for viewing the pelvic organs, most of the difficulties have been solved.

My own particular interest has been in abnormalities of the Fallopian tubes.

We have, for several years, been doing tubal plastic operations. These operations have been largely discredited, and I think that they can achieve success only if the pre-operative diagnosis is carried on in a very meticulous manner. It has been my experience with the use of the culdoscope and the injection of dye into the uterus under pressure that very accurate diagnosis of tubal abnormalities can be made. I think that with experience one can very definitely pick those cases where success from tubal plastic operations can be achieved. Those that are absolutely hopeless can then be discarded. This technique has become a house staff procedure. It is not difficult to teach the members of the house staff to use this instrument. I could not say offhand how many times in a year it has been used but I imagine in the neighborhood of 50. To date we have had no serious difficulties. One of the interesting things, it seems to me, is the way in which a pathological diagnosis is made with the culdoscope.

I do not know what Dr. Decker's experience has been, but mine is that you get no real interpretation of size of an abnormality. An ovarian cyst may be either large or small, depending upon the distance that the culdoscope is from the cyst. In general it tends to reduce the size. However, the diagnosis is made by color as far as I am concerned and by translucency. It is this point that requires teaching as far as the house staff is concerned. It is not the kind of instrument that one can pick up and make an accurate diagnosis the first time, or the fifth time, but, on the other hand, the technique is not so complicated that one cannot learn it in a reasonable length of time.

I was interested in Dr. Decker's use of local anesthesia. We found that the patients in general behave a little better with the use of high dilution, low spinal, with small dosage, so that the anesthesia does not impair the motor power. I would like to hear Dr. Decker's comment on that.

DR. EDWARD A. BULLARD.—Culdoscopy is a valuable diagnostic technique that should be employed in every gynecologic service. Heavy sedation and firm placement of the patient make her indifferent to the discomfort of the knee-chest position. With aseptic precautions and careful selection of suitable cases there should be no shock and no infection. Obviously the method is useless and contraindicated in the presence of large tumors or a frozen pelvis but in the differential diagnoses of ectopic pregnancy, salpingitis, cystic ovaries, endometriosis, and small tumors it has great value. Often one sees with amazing clarity all the pelvic organs except the bladder and the anterior surface of the uterus.

Many an unnecessary laparotomy will be avoided after the correct diagnosis has been made by the culdoscope.

DR. RALPH L. BARRETT.—May I ask Dr. Decker to tell us a little more of what can be seen with the culdoscope? I would like to know what is actually visible in the pelvis. Are the structures sufficiently well visualized to be of great benefit in diagnosis and is the method entirely free from danger? I understand that of 91 cases reported by the previous discussant, there were two patients with sufficient morbidity to necessitate hospitalization and treatment. It seems to me that if 91 abdomens were opened by

incision, not only would the physician be in a position to carry out indicated surgery, but the visualization would be much more complete and probably the morbidity no greater.

DR. HENRY S. ACKEN, JR.—I would like to ask two questions: first, whether Dr. Decker has had any experience with carcinoma of the ovary in this examination, and, second, whether he feels that curettage may be done in conjunction with this, and, if so, which he would prefer to do first, the culdoscopy or curettage.

DR. THOMAS J. PARKS.—Dr. Decker makes a point of being careful to express the air from the peritoneal cavity before he withdraws the instrument. Normally there is negative pressure in the abdomen and, because of this, some of us have felt that there is less abdominal distention when the peritoneal cavity is deflated prior to closure of the peritoneum in pelvic surgery and cesarean sections.

DR. DECKER (Closing).—The question has been asked, "What, actually, can you see through the instrument?" This question has often been asked before, and on occasion the skeptic inquires, "What did he say he saw?"

As I stated in the paper, you can, for example, see the ovary accurately enough to introduce an aspirating needle into the stigma of a follicle and aspirate the contents. The exact condition of the fimbriae can be observed in detail, and bands of adhesions about them can be located accurately enough to be divided and pushed away. The technique of telescopic observation requires some practice so that objects can be brought into the field readily and completely observed.

The most convincing evidence of ability to see is obtained by looking through a culdoscope. It is difficult to get good pictures in color through the culdoscope because of the intense light required for short exposures.

Dr. Buxton has asked if we use carbon dioxide. Spontaneous air pneumoperitoneum of 1,500 to 1,800 c.c. occurs during cul-de-sac puncture in the knee-chest position. At first we believed the air would cause considerable distress, and for this reason the instrument was devised so that carbon dioxide could be substituted for air. Since most of the air can be removed from the peritoneal cavity by pressure on the abdomen, we seldom use carbon dioxide except when we want to be very sure the patient may leave the hospital soon after the examination.

As for anesthesia and premedication, we have made the puncture without anesthesia, but usually local Novocain infiltration of the septum is used. We always use premedication; usually 75 mg. of Demerol have been sufficient to overcome apprehension. Frequently the women with sterility problems are not greatly disturbed by the procedure and register no complaints.

Dr. Bullard mentioned that he was able to see only the posterior surface of the uterus. It is possible to employ telescopes with an oblique or retrograde vision lens so that all surfaces come into view.

I have been asked whether a curettage could be done in conjunction with culdoscopy. This may be done, but I suggest that the culdoscopy precede the curettage because the position might allow blood and endometrial tissue to drain into the peritoneal cavity through the tubes or the colpotomy wound. We have also used tubal insufflation in conjunction with culdoscopy. When other types of procedure are combined, we use a saddle block type anesthesia, using 2.5 per cent solution of Novocain. The dilute solution does not involve the myelinated fibers so that there is no loss of motor control, and the knee-chest position may be voluntarily maintained. With this type of anesthesia, we were able to use very high pressure during visualization without discomfort.

With this inflation type of anesthesia and the table position we employ, it has not been necessary to use the surcingle type of support Dr. Bullard has described.

MULTIPLE CANCER, PRIMARY IN THE FEMALE GENITALS AND OTHER SITES

ALBERT G. MARRANGONI, M.D., AND RICHARD McKENNA, M.D.,
PITTSBURGH, PA.

(From the Departments of Pathology and Gynecology, Mercy Hospital)

MULTIPLE primary cancers in the same individual are no longer a medical curiosity. These multiple lesions have been known to group themselves in organs that are part of an anatomic or physiologic system, but they are frequently found in sites that have no particular relationships.

Warren and Gates^{1, 2} found 194 instances of multiple primary malignant growths in 2,829 autopsies—an incidence of 6.8 per cent. They felt that a patient with one carcinoma was more likely to develop a second cancer than would be expected normally. They found that an average interval of 3.2 years elapsed between the appearance of the individual neoplasms.

In studying multiple primary cancers of the female genitals, it is often difficult to distinguish between metastatic new growths and primary new growths. This is especially true in regard to uterus and ovary. In Warren and Gates' series, 0.8 per cent of the lesions involved the female genitals. Andrews and Nicholls³ have reported independent co-existing tumors of the uterus and ovary. Dockerty and Mussey⁴ have reported fifteen cases of adenocarcinoma of the uterus associated with granulosa-cell and theca-cell tumors of ovary. On the other hand, Falls⁵ reviewed thirty-nine cases of feminizing tumors of the ovary with only one instance of carcinoma of the fundus of the uterus. Pratt, in discussing Stohr's⁶ article on granulosa-cell tumor, stated that he reviewed 135 cases of adenocarcinoma of the uterus and found no cases of granulosa-cell tumor of the ovary associated with this type of malignancy. We have reviewed 193 cases of adenocarcinoma of the uterus with no instances of granulosa-cell tumors.

The management of multiple primary cancer may, at first, be extremely complex. In those cancers which appear synchronously, it may be difficult to decide which tumor deserves first consideration, or if both should be treated at once. In the treatment of metachronous lesions, the problem is less difficult since there may be more deliberate treatment for the second primary.

The possibility of survival diminishes with the advent of each new cancer capable of metastasizing. Yet it seems more evident as our experience accumulates that radical therapy for such aggression has been met with surprisingly favorable results. The occurrence of one, two, or three primary cancers does not necessarily contraindicate radical treatment for each cancer. For example, an adenocarcinoma of the rectum has been treated by abdominal perineal resection; a later carcinoma of the uterus should be treated by panhysterectomy and bilateral salpingo-oophorectomy, following adequate radium therapy, without altering the patient's ultimate prognosis.

In this study we have reviewed all the cancers of the female genitals occurring in the last ten years at Mercy Hospital in an attempt to determine the incidence of multiple primary cancers of the female genitals. We have also attempted to correlate the prognosis in relation to treatment for each cancer.

Criteria for Multiplicity

Criteria for diagnosis of multiple cancers must be clearly defined. Billroth states that only those primary cancers with individual metastases can be considered. However, it has been generally agreed that the distinction can be made when the tumors have entirely different histological characteristics.⁷ We are reporting fifteen cases meeting this criteria and these are classified as having positive evidence of multiple primary cancers. There were three cases which were considered doubtful and are not included in this series.

Compilation of Cases

In 618 cases of carcinoma of the female genitals observed at Mercy Hospital between 1940 and 1950, there have been fifteen instances in which there were one or more separate primary malignant tumors of the female genitals—an incidence of 2.4 per cent (Table I). There were two triple primaries.

The sites of the separate malignant growths in our series are listed in Table II. There were three cases of carcinoma of the ovary associated with carcinoma of the uterus, six cases of carcinoma of the colon associated with that of the ovary and uterus, three cases of carcinoma of the breast associated with the ovary and uterus and one case of carcinoma of the kidney associated with carcinoma of the cervix. The two triple malignancies included breast, sigmoid, and cervix; and colon, ovary, and uterus (Table II).

In discussing multiple primary malignant growths, the time relationship between the appearance of the tumors is of interest. In this report, the cancers are synchronous, if the interval of time between the establishment of the first primary tumor and the detection of the second was less than six months; metachronous, if more than six months. In our fifteen cases, the cancer in the female genitals was synchronous in six instances, and in nine cases the second primary appeared after six months from the time the first primary was treated. The average time interval in this series was 1.8 years.

TABLE I. MULTIPLE PRIMARIES ASSOCIATED WITH CANCER OF FEMALE GENITALS

Total cases of cancer of female genitals	618
Total multiple primaries	15
Incidence	2.4%

Diagnosis

With a female patient who has a known cancer, other than in the genitals, the problem of detecting a genital cancer often requires considerable clinical study. As in the diagnosis of any disease, the history and physical examination are always important. In only two cases was cancer found in the immediate family, but this item on the patients' histories was frequently incomplete. Postmenopausal bleeding and bleeding between periods were the most frequent symptoms, occurring eight times. It is our feeling that a complete and careful pelvic examination should be carried out in every female patient with cancer, regardless of its site.

Diagnostic curettage and biopsy of the cervix may be reserved for those with positive findings on pelvic examination or suggestive history of pelvic pathology. In two cases, a curettage was not performed and subtotal hysterectomy was performed for what subsequently revealed itself to be adenocarcinoma of the fundus. Had a curettage been performed, or had the specimen been opened at the operating table, a total hysterectomy would have been the treatment of choice.

Although cytological studies were not performed in this series of patients, it must be considered a useful adjunct to diagnosis. The ages in this series varied from 32 to 69 years, with the average age being 49.8 years. The youngest patient had an adenocarcinoma of the rectum and a papillary carcinoma of the right ovary. The oldest patient had an adenocarcinoma of the colon and an adenocarcinoma of the fundus.

TABLE II. MULTIPLE PRIMARIES ASSOCIATED WITH CANCER OF FEMALE GENITALS

DOUBLE PRIMARY	
Breast	2
Colon	3
Ovary	4
Rectum	3
Kidney	1
Total	13
TRIPLE PRIMARY	
Breast and colon	2
Total cases	15

Treatment

Of the fifteen cancers of the female genitals in this series, three had pan-hysterectomy and bilateral salpingo-oophorectomy; four had subtotal hysterectomy and bilateral salpingo-oophorectomy; one had radium therapy; one had radium plus x-ray therapy; one had oophorectomy; one had bilateral salpingo-oophorectomy; and four had no treatment because of the advanced stage of the disease when the diagnosis was made (Table III).

TABLE III. SUMMATION OF CASES OF MULTIPLE CANCERS ASSOCIATED WITH CANCER OF THE FEMALE GENITALS

PATIENT	AGE (YEARS)	FIRST PRI- MARY	TIME INTERVAL (YEARS)	SECOND PRI- MARY	FIRST SYMPTOM	DIAGNOSIS ESTABLISHED	FOLLOW- UP*
L. L.	41	Ovary	0	Uterus	Pain in back	Laparotomy	N.E.D.
N. N.	62	Colon	0	Ovary	Abdominal cramps	Laparotomy	D.O.D.
G. K.	35	Colon	0	Uterus	Prolonged menses	Laparotomy	N.E.D.
M. L.	69	Colon	0	Uterus	Vaginal bleeding	Curettage	D.O.D.
T. R.	39	Ovary	0	Uterus	Swelling of abdomen	Laparotomy	N.E.D.
V. G.	42	Ovary	0	Uterus	Spotting	Laparotomy	N.E.D.
L. G.	56	Rectum	7	Uterus	Bleeding	Curettage	N.E.D.
P. W.	32	Colon	1	Ovary	Pain	Laparotomy	D.O.D.
M. M.	35	Colon	2	Ovary	Bleeding	Laparotomy	D.O.D.
E. H.	47	Breast	2	Ovary	Bleeding	Laparotomy	D.O.D.
M. S.	52	Breast	1	Uterus	Bleeding	Curettage	Metas- tases
M. S.		Cervix	8 months	Kidney	Pain	Autopsy	D.O.D.
C. B.	60	Breast	10 months	Ovary	Swelling of abdomen	Autopsy	D.O.D.
A. R.	55	Breast	13	Cervix	Bleeding	Biopsy	D.O.D.
V. H.	50	Uterus	8 months	Ovary	Pain	Laparotomy	N.E.D.
		Colon					

*N.E.D. No evidence of disease.

D.O.D. Died of disease.

Prognosis

In our series, six patients are living and well, free of metastasis, one living with metastasis, while eight have died of their disease. As mentioned above,

four of these patients had no treatment. The ultimate prognosis of these patients does not depend on the multiplicity of their malignancies but rather on the extent of their disease and the method of treatment. Two cases will be described in detail:

CASE 3.—G. K., aged 35 years, para i, gravida i, consulted a physician in November, 1946, because of prolonged periods (ten to sixteen days) of one year's duration. She had noted blood in the stools for three months. At operation, an adenocarcinoma of the sigmoid was resected and a hysterectomy and left salpingo-oophorectomy were performed for what was thought to be a degenerating submucous fibroid. When the pathological report revealed adenocarcinoma of the fundus, 1,200 mg. hr. radium were given to the cervical stump.

Comment: This is an example of a synchronous lesion treated by radical therapy. The patient is living and well today (six years). There were no metastases in the regional lymph nodes about the sigmoid tumor, which undoubtedly had much to do with the favorable outcome. Postoperative radium therapy to the cervical stump was also well advised.

CASE 10.—E. H., aged 47 years, para 0, gravida 0, consulted a physician Nov. 15, 1947, because of a lump in right breast of six months' duration. Radical mastectomy was performed for a colloid carcinoma, Grade 2. There were no metastases. The patient noted vaginal bleeding for two weeks in January, 1949, and a mass in the left adnexal region was palpable. A subtotal hysterectomy and bilateral salpingo-oophorectomy were performed for a papillary carcinoma of the left ovary. The patient died of her disease Jan. 11, 1951.

Comment: This is an example of a metachronous lesion in which the patient died of her disease. Although it cannot be stated positively in any one case, it would have been advisable to perform a total rather than subtotal hysterectomy in this case, and post-operative x-ray therapy may have been indicated. Nunnell and Taylor⁸ state that survival curves for surgery plus x-ray in the more malignant histological types of tumors of the ovary are better than the survival curves for surgery alone.

Summary

1. In 618 cases of cancer of the female genitals, there were fifteen multiple primary cancers in which the female genitals were the site of one of the tumors.
2. There were six instances of synchronous, and nine of metachronous multiple cancers. Two triple cancers (one involving breast, sigmoid, and uterus; and one involving uterus, ovary, and colon) are included.
3. The relative importance of the methods of establishing a definite diagnosis of female genital cancers has been discussed. The value of diagnostic curettage and exfoliative cytology have been emphasized, particularly in female malignancies of all types.
4. There should be no defeatism because of the appearance of multiple primary cancers. Rather, aggressive measures directed toward determination of the nature of each new growth and eradication of it must be instituted.

References

1. Warren, S., and Gates, O.: *Am. J. Cancer* 16: 1352, 1932.
2. Warren, S., and Ehrenreich, T.: *Cancer Research* 4: 554, 1944.
3. Andrews, C. J., and Nicholls, R. B.: *AM. J. OBST. & GYNEC.* 53: 75, 1947.
4. Dockerty, M. B., and Mussey, E.: *AM. J. OBST. & GYNEC.* 61: 147, 1951.
5. Falls, F. H., Ragins, M. S., and Goldenberg, M.: *AM. J. OBST. & GYNEC.* 57: 1007, 1949.
6. Stohr, G.: *AM. J. OBST. & GYNEC.* 43: 586, 1942.
7. Tullis, J.: *J. Lab. & Clin Med.* 27: 588, 1942.
8. Munnell, E. W., and Taylor, H. C.: *AM. J. OBST. & GYNEC.* 58: 943, 1949.

A CRITICAL STUDY OF THE EFFICACY OF JELLY AS A CONTRACEPTIVE

RUTH FINKELSTEIN, M.D., ALAN GUTTMACHER, M.D., AND
RAYMOND GOLDBERG, M.D., BALTIMORE, MD.

(From the Contraceptive Clinic of the Sinai Hospital)

THE Sinai Hospital of Baltimore, a general voluntary institution, has conducted an intramural contraceptive clinic since 1942. In the early years many methods were prescribed simultaneously, the method selected depending upon circumstances and the patient's wishes. The occlusive vaginal diaphragm with jelly or cream was most frequently recommended. A few years after the clinic had opened it became apparent that contraceptive clinics of the same type were abundant, but too few were carrying out critical investigations of a particular method. Therefore, we proposed to undertake a meticulous study of some uniform, single method for a total clinic population, irrespective of patient preference. The method selected for study was jelly alone. Several similar jelly studies had been done, but some were weakened by inadequate critique and follow-up. A three-year study was planned, and began Feb. 1, 1948.

All married clinic patients who delivered during the two-year period, Feb. 1, 1948, to Feb. 1, 1950 and who desired contraceptive advice were enrolled in the study. None was added after Feb. 1, 1950, but the study was not concluded until Feb. 1, 1951, so that those who did not drop out prematurely were followed from 12 to 36 months. During the two-year period, 1948 to 1950, 1,826 patients were seen in the six weeks post partum clinic. Jelly* was offered to all desiring contraceptive advice; six hundred five accepted. Of the others, some did not wish to use contraception at all, others preferred the method they had employed previous to impregnation, while still others desired referral to clinics prescribing the diaphragm. They lacked faith in jelly alone, having heard favorable reports of its efficacy only when used in combination with the diaphragm.

Of the six hundred five patients enrolled in the study, 52 per cent were Catholic, 43 per cent Protestant, and 5 per cent Jewish. Thirty-six per cent had just been delivered of a first living child, while 64 per cent had two or more living children when the study was initiated.

These married, recently puerperal patients were given a thorough post-partum examination including visualization of the cervix with cauterization if necessary, replacement of a retroposed uterus and the insertion of a Smith-Hodge pessary. A short history was taken by a physician and the patient instructed in the use of contraceptive jelly. She was taught to insert the jelly-filled applicator as far up as it would go into the vagina, to withdraw it about an inch and then push the plunger, which delivered 5 c.c. of jelly in the region of the cervical os. This was to be done immediately preceding coitus. A post-coital douche was not permitted until the following morning, or until a minimum of six to eight hours had intervened after intercourse.

Of the six hundred five who accepted the jelly, sixty-eight moved away, making their complete follow-up impossible. One hundred sixty-six rejected the method almost immediately because (1) they had heard that the use of "jelly without the diaphragm is not a safe contraceptive method," or (2) they found the jelly "too messy" and it "leaked out of the vagina." To investigate

*Throughout this study an A.M.A. Council accepted jelly (Ramses) was used exclusively.

the latter complaint we incubated some jelly at 37° C. for twenty-four hours and found no alteration in its viscosity.

There is an appalling lack of uniformity in the rules and standards employed for the scientific evaluation of contraceptives. All patients are included in this study who used the jelly method more than two months. We did not count any patient an active user until she had had two menstrual periods after being given supplies, thus eliminating those pregnant at the initiation of the study, and also patients so halfheartedly interested that they simply contemplated the use of the method rather than actually employing it.

The patient was told to repeat the instructions to the physician and encouraged to ask questions. She was then provided with two tubes of jelly and the standard 5 c.c. nozzle. A minimum charge for materials was made to those able to pay. This was not done to help support the study; but it was felt that the patient who paid would take better care of her supplies and use them more regularly. Each patient was told how to contact the full-time social worker employed by the project if she suddenly needed additional supplies. Otherwise the worker visited her home every third month, interviewed her, and left additional tubes of jelly.

Those eliminated for use less than three months are summarized:

NUMBER OF PATIENTS	MONTHS USED	PATIENT MONTHS	PREGNANCIES
20	1	20	4
25	2	50	8
—	—	—	—
45	3	70	12

Eliminating these forty-five patients the results are calculated on the three hundred twenty-five patients who used contraceptive jelly alone from three to thirty-six months. As can be noted from Table I the unplanned pregnancies are divided into method failures and patient failures. The former classification is reserved for patients who claimed to have used the method each time coitus was practiced, the latter for those frankly admitting an occasional or frequent omission of use.

The results of the study are summarized in Table I and need no further elucidation.

Since it is impossible to eliminate periods of irregular use from the total period of exposure, the last column "total failures" probably represents the most significant index of contraceptive effectiveness.

Failures

All investigators agree that motivation, the sincere, urgent, uncomplicated desire to remain nonpregnant, is one of the most important, if not the most important factor in a couple's successful use of any contraceptive technique. It may smack of heresy, but it is likely that motivation is more important in most instances than the fact that the couple uses method "A" or method "B." Two factors possibly related to motivation, religion and parity, were available to us for analysis. It is recognized that these are not the only factors affecting contraceptive motivation but they could be important factors.

RELIGION, WHOLE GROUP			RELIGION, METHOD FAILURE			RELIGION, PATIENT FAILURE		
FAITH A	FAITH B	FAITH C	FAITH A	FAITH B	FAITH C	FAITH A	FAITH B	FAITH C
52%	43%	5%	61%	39%	0	69%	31%	0

The above suggests that the Faith A group has mixed feelings about contraception, feelings which affect their motivation and perhaps penalize the effectiveness of the jelly technique.

It appears that jelly alone is more effective as a contraceptive among patients of lower parity. This of course could be caused by different degrees of motivation, or simply by anatomy. The jelly might be confined to the region

PARITY, WHOLE GROUP		PARITY, METHOD FAILURE		PARITY, PATIENT FAILURE	
ONE CHILD	MORE THAN ONE	ONE CHILD	MORE THAN ONE	ONE CHILD	MORE THAN ONE
36%	64%	16%	84%	28%	72%

of the external os more successfully in the less relaxed vagina. The low incidence of patients with one child among the method failures gives some basis for this hypothesis.

TABLE I. PREGNANCY RATE OF PATIENTS WHO USED METHOD 3 MONTHS TO 3 YEARS

The pregnancy rate is calculated from the formula:

R— $1200 \times \frac{\text{pregnancies}}{\text{months of exposure}}$ —Pregnancy rate per 100 patient years of exposure

R—(method failures)— $1200 \times \frac{46}{5103} = 10.82$

R—(total failures)— $1200 \times \frac{71}{5103} = 16.70$

NO. PTS.	MOS. USED	PT. MOS.	METHOD FAILURES	PT. FAILURES	TOTAL FAILURES
29	3	87	3	0	3
12	4	48	3	5	8
20	5	100	3	4	7
17	6	102	3	3	6
14	7	98	6	1	7
12	8	96	2	4	6
15	9	135	3	1	4
7	10	70	3	1	4
7	11	77	0	1	1
8	12	96	2	0	2
8	13	104	1	1	2
19	14	266	1	0	1
11	15	165	1	0	1
16	16	256	4	1	5
13	17	221	1	1	2
6	18	108	2	0	2
6	19	114	2	0	2
4	20	80	1	1	2
8	21	168	1	1	2
4	22	88	1	0	1
10	23	230	0	0	0
5	24	120	0	0	0
4	25	100	0	0	0
8	26	208	0	0	0
11	27	297	0	0	0
6	28	168	1	0	1
8	29	232	2	0	2
6	30	180	0	0	0
2	31	62	0	0	0
4	32	128	0	0	0
5	33	165	0	0	0
9	34	306	0	0	0
4	35	140	0	0	0
8	36	288	0	0	0
326	663	5,103	46	25	71*

*Of the 71 failures, 18 used the method less than six months.

Comparisons

Since not all authors use the same criteria for reporting effectiveness or ineffectiveness of various contraceptives it is difficult to compare results with those of other investigators. However, by calculations from published data, Tietze¹ has compiled a table giving a comparison of the results achieved by those using jelly or cream alone in different communities.

The widespread range of effectiveness demonstrated by the several different reports is more apparent than real. So much depends on the quality of follow-

up employed by the investigators. Of equal or even greater importance is the population sample which constitutes the study material. Their intelligence, motivation, parity, and ready access to new supplies all affect success or failure. The unweighted mean pregnancy rate of the ten studies is 22.3 per 100 years of exposure the median rate lies between 17 and 20.

LOCALITY AND LITERATURE REFERENCE	YEARS OF EXPOSURE	NUMBER OF PREGNANCIES	PREGNANCY RATE
Spartanburg, S. C.	160	15	9
Philadelphia	60	9	15
New York City	203	33	16
Baltimore*	425	71	17
Lee County, S. C.	66	11	17
Chicago	241	47	20
Kentucky Counties	204	41	20
Kershaw County, S. C.	484	152	31
Logan County, W. Va.	938	354	38
Puerto Rico	77	31	40

*The figures credited to Baltimore are those from the current study.

We determined to compare the efficacy of the suppository as a contraceptive with that of jelly alone. This decision was determined by the fact that the Eastman-Siebels² study on the suppository had sufficient features in common with our own jelly study to make comparison valid. Both studies originated in the same urban community, both were carried out on postpartum patients and both were accompanied by a careful follow-up. To make the studies exactly comparable we had to eliminate from our study, as did Eastman, those who used the method for less than six months.

Eastman's² suppository series for patients using the method six months or longer has a total pregnancy rate of 16.2 per hundred woman years of exposure, while our jelly study, a total pregnancy rate of 13.1.* The method failure rate in the Eastman suppository study was 11.1; our jelly method failure rate, 9.1.

Total pregnancy rate	$\frac{1200 \times 53}{4868}$	or 13.1
Pregnancy rate due to Method Failure	$\frac{1200 \times 37}{4868}$	or 9.1

Summary

1. A meticulous three-year study was carried on to determine the efficacy of jelly alone as a contraceptive agent.

2. There were 16.7 unplanned pregnancies per 100 years of exposure in three hundred twenty-five postpartum clinic patients using jelly alone as a contraceptive. In the two hundred sixty-four patients who used the method six months or longer, the unplanned pregnancy rate was 13.1 per 100 years of exposure.

3. It is likely that religion and parity affect the rate of success, the former through the mechanism of motivation, the latter through the avenue of anatomy.

4. Jelly alone appears to have a failure rate somewhat similar to that of the suppository as reported by Eastman and Siebels.²

References

1. Dickinson, R. L.: Techniques of Conception Control, ed. 3, Baltimore, 1950, The Williams and Wilkins Company.
2. Eastman, N. J., and Siebels, R. E.: J. A. M. A. 139: 16, 1949.

*Computation of failure rate for patients using jelly method six months or longer, per hundred years of patient exposure.

AN EVALUATION OF SURFACE SPONGE BIOPSY IN A CANCER DETECTION CLINIC WITH SPECIAL REFERENCE TO THE USE OF AN ENDOMETRIAL SPONGE BIOPSY FORCEPS*

BERNARD DIAMOND, M.D., NATHAN MITCHELL, M.D., F.A.C.P., AND
EDWARD BLUM, M.D., BROOKLYN, N. Y.

(From the Departments of Obstetrics and Gynecology and Pathology, Beth-El Hospital)

SINCE the introduction by Papanicolaou¹ of exfoliative cytology as a specialized method of cancer diagnosis and detection, particularly of neoplasms of the female generative tract, the trend has been to the adoption of more selective methods. In the diagnosis of cervical cancer, direct cervical smears, Ayre's spatula scraping,² and Gusberg's³ conization biopsy have largely replaced the original vaginal pool secretion technique. In 1948 Gladstone⁴ introduced the surface sponge biopsy procedure which has achieved a wider acceptance by pathologists because of the ease of its performance and the familiar medium which it utilizes. Gladstone has used the sponge biopsy in the diagnosis of cervical cancer, with good results. The practicability of the sponge biopsy has been further substantiated by Angrist and associates.⁵

Most authors report a higher incidence of accurate diagnoses in cervical cancer (96.8 per cent) than in uterine fundal carcinoma (90.7 per cent).⁶ The statement has been made⁷ that "the routine diagnosis of cancer of the uterus by examination of the vaginal smear has definite limitations, *particularly in cases of endometrial cancer.*" Ayre has advocated the use of endometrial aspiration smears, and Palmer and co-workers⁸ have used the endometrial aspiration biopsy utilizing the Novak suction curette as an ideal office procedure in order to facilitate the early diagnosis of endometrial carcinoma. It seemed advantageous to apply a more selective method of sampling of the endometrium in a cancer detection center. For this purpose a specially designed sponge biopsy forceps was employed.

Materials and Methods

With the exception of the four cases of endometrial carcinoma to be described more fully below, the material comprising this report was gathered from women attending the Cancer Detection Clinic of the Beth-El Hospital. Because of limitations in personnel and time, it was predetermined that the sole method for studying exfoliative cytology would be the surface sponge biopsy as introduced by Gladstone. The increased volume of biopsy material has not necessitated an increase in the technical staff of the laboratory. More important and in sharp contrast to the time-consuming procedure of examining a like number of vaginal, cervical, or endometrial smears, the amount of time required of the pathologist in examining these sponge biopsies (either gelatin or cellulose) was not in excess of that ordinarily required in reading formal tissue biopsies.

*Presented at a meeting of the Brooklyn Gynecological Society, Oct. 17, 1951.

A cervical sponge biopsy was performed on each woman who attended the clinic. After several months, endometrial sponge biopsies were performed as time permitted, by the use of a specially designed instrument (Fig. 1). The position of the uterus was determined by bimanual examination, using water as a lubricant. After visualization of the cervix, routine cervical and endocervical sponge biopsies were taken. A small square of the sponge material (either cellulose or gelatin) was firmly attached to the tip of the biopsy forceps by moving the outer collar upward, thus approximating the teeth of the instrument tip. The instrument was then gently pushed into the endocervical canal and into the fundus of the uterus. With the exception of approximately 5 per cent of the patients in the older age groups, passage into the endometrial cavity was then easily effected. The sponge was rubbed over all aspects of the endometrial cavity, with care taken to explore into the cornua. It was noted that pain and spotting after instrumentation were minimal. In three of the 97 cases, slight bleeding was reported by the patients for periods ranging from 24 to 72 hours after the biopsy was performed.



Fig. 1.—Endometrial sponge biopsy forceps in closed position, indicating proper level for outer collar.

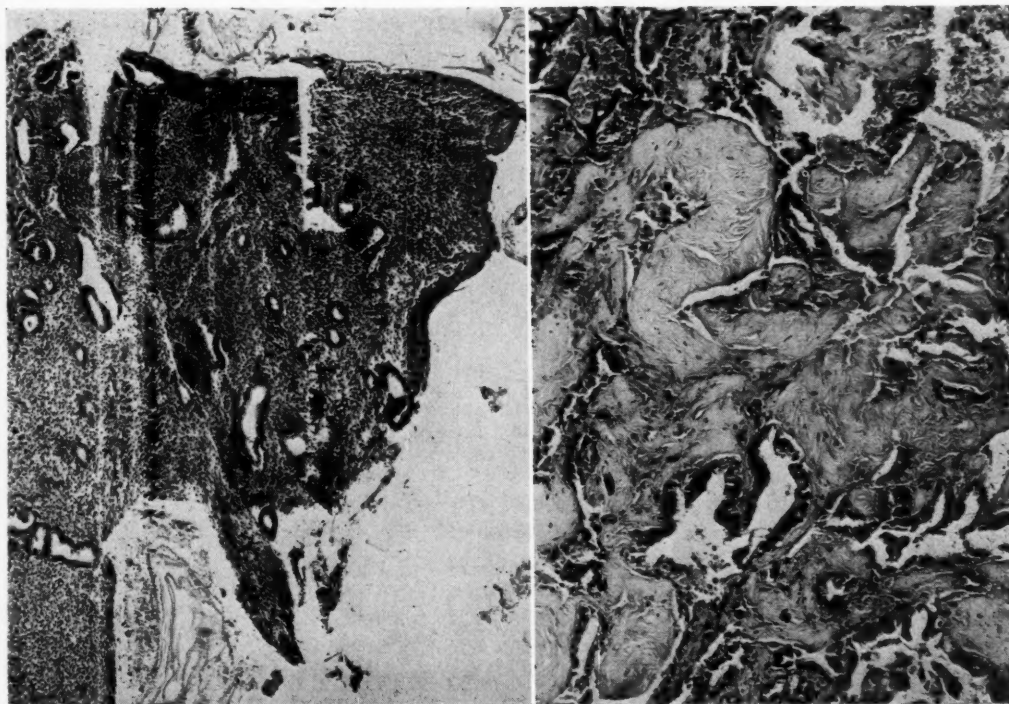


Fig. 2.

Fig. 3.

Fig. 2.—Large fragment of endometrium obtained by sponge biopsy forceps. Fragments of the cellulose sponge are seen in upper portion of photograph.

Fig. 3.—High-power view of papillary adenocarcinoma diagnosed by sponge biopsy. The stroma of the neoplasm is hyalinized. Small fragments of the gelatin sponge are seen in the upper left margin.

Results

During the time covered by this preliminary report 666 cervical and 97 endometrial sponge biopsies were performed. Of the 666 cervical biopsies, one was reported as positive for cancer. This case was confirmed by routine surgical pathologic study. Two additional cases were reported as having atypical cells, but subsequent formal biopsy proved them to be negative. The remaining 663 cases were reported as negative, but no subsequent follow-up study is as yet available. In each of the 97 endometrial sponge biopsy specimens, recognizable fragments of endometrial tissue were identified. The size of the fragments varied, but usually several endometrial glands with their mantle of stroma could be seen (Fig. 2). In the larger fragments it was possible to determine the cyclical phase of the endometrium just as with formal biopsy. Up to the present time, no case of early asymptomatic endometrial cancer has been discovered. In order to test the validity of this method utilizing the sponge biopsy forceps, endometrial sponge biopsies were performed on several hospitalized patients with the presenting complaint of vaginal bleeding. In three of these cases, a diagnosis of endometrial adenocarcinoma was established primarily on the sponge biopsy (Fig. 3). In an additional instance, a diagnosis of adenoacanthoma was made on the basis of the tissue obtained by the endometrial sponge biopsy forceps. The latter four cases were confirmed by formal endometrial biopsies.

Summary and Conclusions

The method of surface sponge biopsy as introduced by Gladstone has been applied to the study of the female generative tract in a Cancer Detection population. Both cervical and endometrial cytology were investigated, the latter by means of a specially designed endometrial sponge biopsy forceps. In the series of 666 cervical biopsies, a single case of intraepithelial epidermoid carcinoma was found. The 97 endometrial sponge biopsies failed to reveal early asymptomatic endometrial cancer.

The advantages of the method described in this report are the ease of performance of the endometrial sponge biopsy, the relative absence of pain and bleeding after biopsy, and the practicability of examining large numbers of women at a single clinic session. The sponge biopsy forceps method may also be utilized in office practice for rapid diagnosis of endometrial cancer where early hospitalization is not feasible.

The authors wish to thank the Upjohn Company for their generous supply of Gelfoam in the early part of this study, Mr. Reginald Bates of the Sklar Instrument Company, for his aid in producing the final model of the forceps, and Mr. Stanley P. Clurman, M.E., for preparing the first model of the instrument.

References

1. Papanicolaou, G. N., and Traut, H. F.: *Diagnosis of Uterine Cancer by Vaginal Smear*, New York, 1943, The Commonwealth Fund.
2. Ayre, J. E.: *Canad. M. A. J.* **51**: 17, 1944.
3. Gusberg, S. B.: *AM. J. OBST. & GYNEC.* **57**: 752, 1949.
4. Gladstone, S. A.: *Am. J. Med.* **5**: 849, 1948.
5. Rich, J., Angrist, A. A., and Carpenter, F.: *AM. J. OBST. & GYNEC.* **59**: 1029, 1950.
6. Meigs, J. V., Graham, R. M., Fremont-Smith, M., Janzen, L. T., and Nelson, C. B.: *Surg., Gynec. & Obst.* **81**: 337, 1945.
7. Leaflet # 23, New York State Ass'n. Pub. Health Labs., Albany, N. Y., Sept., 1949.
8. Gusberg, S. B., and Graham, D. A.: *AM. J. OBST. & GYNEC.* **59**: 1053, 1950.
9. Palmer, J. P., Kneer, W. F., and Eccleston, H. H.: *AM. J. OBST. & GYNEC.* **60**: 671, 1950.

THE RETURN OF REPRODUCTIVE CAPACITY FOLLOWING SPONTANEOUS ABORTION*

CHARLES LEAVITT SULLIVAN, M.D., BOSTON, MASS.

(From the St. Elizabeth's Hospital)

THE normal expectancy of sequential events is intercourse, pregnancy, and the delivery of a healthy baby at term. The intrusion of a spontaneous miscarriage into this cycle is productive to the patient of a sense of frustration and depression which is translated into psychophysical complaints. It is interesting to note just how much the simple uncomplicated spontaneous abortion debilitates the average woman, who never expects this common calamity to enter her personal sphere. Upon the quick recovery which generally ensues from this depression, there naturally arise, first, the question as to the cause of the misadventure, and, second, the instinctive desire again to attempt reproduction. In the mind of the patient the cause is always physical and never anatomic, physiologic, or dietetic. This study was undertaken to determine the time of and the efficiency of the reproductive capacity following spontaneous abortion.

Williams,¹ by means of endometrial biopsy, has beautifully described the regeneration of the uterine mucosa following term delivery and thus by indirection the hormonal effects that such changes portray. By the same method and approach, Rutherford and Mezer² reported on nine cases of spontaneous abortion, and, guided by the experience of Reid,³ urged immediate attempt at reimpregnation following the event in the hope of obtaining a good pregnancy. The established physiological concept of a thermogenic response to the ovarian production of progesterone was the method used in this study.⁴

Material

A total of seventy-five women were followed by means of daily basal body temperatures from the onset of their spontaneous abortion or curettage to the first menstrual period thereafter. Sixty-four women had a curettage and eleven were adjudged to have emptied their uteri completely. In all cases, the shortest and longest intervals to the return of the menses were twenty-one and fifty-nine days, respectively. Seventy-five per cent started to flow between four and one-half and five and one-half weeks following the abortion, with the highest percentage at five weeks. By the end of six weeks 95 per cent had had their first flow. In the eleven cases without a curettage, this was accomplished between thirty-three and thirty-nine days. The first flow was ovulatory in type in sixty-nine women, or roughly 90 per cent, with five patients following curettage failing to ovulate and one anovulatory who had no intervention at the time of abortion. The days of the thermogenic response, by indirection denoting ovulation, in those cases with a curettage, had a span of thirteen to forty-seven days with 75 per cent occurring between the twenty-first and twenty-

*This study was aided by a grant in research by Schering Corporation.

eighth day. The span of those with no curettage ran between eighteen and eighty-seven days, with 50 per cent occurring at the same time as in those with a curettage. The length of the secretory phase in this first cycle, determined by the length of the thermogenic response, varied between four and twenty days, excepting in those women who conceived. Fifty per cent of all secretory phases were shorter than the fourteen plus or minus two days postulated by Hertig and Rock⁵ as normal. The length of this first secretory phase was not affected by the omission or commission of a curettage following abortion, and only 50 per cent of those with or without surgical intervention had secretory phases of the accepted average duration.

Thirty-nine women had intercourse about the time of the rise in basal temperatures with only three conceptions. This is about one-half of the normal pregnancy expectancy rate from intercourse during the fertile period. Following a curettage such exposures were six times more common and resulted in two of the three pregnancies which followed exposures at the first ovulation following abortion. The sole conception following abortion without a curettage occurred on the eighty-seventh day after spontaneous emptying of the uterus. Pregnancies occurred on the seventeenth and the thirty-fourth days following curettage. The one abortion which resulted from the three conceptions was conceived following a curettage.

Following a full-term pregnancy ovulation will occur in about six weeks with the return of the menses in about eight weeks.^{1, 2} This process may be lengthened by lactation, but the time that the return of the ovarian function breaks through is not predictable. Following a spontaneous abortion, in the first trimester, attended by a curettage or not, ovulation occurs in about 75 per cent of cases in three to four weeks, with menses following this event in 95 per cent of cases in four to six weeks. While Rutherford and Mezer² conclude that endometrial evidence indicates that this is a good time for reimpregnation, it has not been the experience in this series.

Rock and Hertig⁶ found one pregnancy that they felt would reach a clinically recognizable form for every six fertile exposures in a selected series of hysterectomies following dated intercourse. The ratio was one pregnancy for every thirteen fertile exposures in the first ovulation following spontaneous abortion in the present series. The reason for this decrease from the normal expectancy of fertility lies probably in the fact that in the first cycle following spontaneous abortion the secretory phase is considerably shortened in over 50 per cent of cases from the usual duration of fourteen plus or minus two days. Before the implantation of a fertilized egg could occur, in the six to ten days post conception usually required, the endometrium may start its catabolic process toward flow, thus making the nidatory site untenable. Markee⁷ has shown that this regression may start any time between two and six days prior to the onset of flow. This time factor may be a more common denominator in sterility and early abortion than hitherto suspected. Chang,⁸ working with the implantation of already fertilized rabbit eggs, has shown that the time of attempted implantation bears a direct relationship to the age of the endometrium in relation both to the chances of successful implants and also to the ultimate outcome of those successfully implanted. Sturgis⁹ postulates an "exhaustion phenomenon" in explaining the failure of further deciduization of the endometrium after sixteen weeks of pregnancy in spite of continued hormonal stimulation. It could be that this tired state continues through the first cycle following abortion, with the endometrium less sensitive to renewed hormonal stimulation, thus decreasing the possibility of nidation. Murphy¹⁰ and Record and McKeon¹¹ have both shown in their studies of congenital anomalies that they occur more commonly in relation either to long periods of

sterility or to a reconception close to a pregnancy ending in spontaneous abortion. It apparently makes no appreciable difference from the standpoint of resumption of ovarian activity whether or not a curettage is done following a spontaneous abortion clinically adjudged completed. It is true that a gentle curettage insures an empty uterus, provides complete material for pathological examination to determine causal factors as well as efficacy of therapy, and lessens the strain of prolonged inevitability. These gains are to be balanced against the risk of any anesthetic and the economic aspect of the procedure to the patient.

Conclusions

1. Routine curettage is not necessary in a clinically complete spontaneous abortion from the standpoint of return of ovarian activity.
2. Ovulation will return in 90 per cent of cases prior to the first menses in four to six weeks, whether a curettage is performed or not.
3. The first ovulation following spontaneous abortion will have a shortened secretory phase in 50 per cent of cases, whether or not a curettage is performed.
4. The first ovulation following spontaneous abortion is about one-half as fertile as in average cycles and exposures to pregnancy before the first flow after abortion probably should be avoided.

References

1. Williams, J. W.: *AM. J. OBST. & GYNEC.* 22: 664, 1931; *J. A. M. A.* 97: 523, 1931.
2. Rutherford, R., and Mezer, J.: *J. A. M. A.* 119: 124, 1942.
3. Reid, D.: Quoted by Rutherford and Mezer.²
4. Palmer, A.: *Obst. & Gynec. Surv.* 4: 1, 1949.
5. Hertig, A., and Rock, J.: *AM. J. OBST. & GYNEC.* 47: 343, 1944.
6. Hertig, A., and Rock, J.: *AM. J. OBST. & GYNEC.* 58: 968, 1949.
7. Markee, J.: in Meigs, J. V., and Sturgis, S. H.: *Progress in Gynecology*, ed. 2, New York, 1950, Grune & Stratton.
8. Chang, M. C.: *Fertility and Sterility* 2: 205, 1951.
9. Sturgis, S. H.: *AM. J. OBST. & GYNEC.* 35: 752, 1938.
10. Murphy, D.: *Congenital Malformations*, ed. 2, Philadelphia, 1947, J. B. Lippincott Company, p. 79.
11. Record, R., and McKeon, T.: *Brit. J. Social Med.* 4: 26, 1950.

1180 BEACON STREET

Department of Case Reports New Instruments, Etc.

NEUROFIBROMATOSIS OF THE CERVIX

LIEUTENANT (JG) JONATHAN G. BUSBY, MEDICAL CORPS, UNITED STATES NAVY,
BETHESDA, MD.

(From the Department of Obstetrics and Gynecology, U. S. Naval Hospital)

NEUROFIBROMATOSIS of the cervix associated with generalized von Recklinghausen's disease has not been previously reported in standard textbooks or the medical literature. This condition, developing after the second pregnancy, is presented in the following case report.

L. H., a 25-year-old white woman, has been followed regularly through two pregnancies by the writer over a period of two years.

When the patient was 22 years old, she first noticed two small skin nodules in the left groin. During her first pregnancy, multiple small nodules began appearing over her back, chest, and abdomen, accompanied by the typical *café au lait* pigmentation of the skin. A biopsy of the skin tumors at this time confirmed the diagnosis of multiple neurofibromatosis, or von Recklinghausen's disease.



Fig. 1.

Fig. 1.—Photomicrograph of neurofibroma of cervix. ($\times 100$.)



Fig. 2.

Fig. 2.—Bielschowsky silver stain of neurofibroma of cervix. ($\times 100$.)

The first pregnancy followed an uneventful course, and the patient delivered a normal female child on July 9, 1949. Her first postpartum examination, 6 weeks later, showed normally involuting pelvic organs, but areas of what appeared to be hyperkeratosis on the cervix.

The patient was next seen in the early months of her second pregnancy in March, 1950. Examination at this time revealed a normal intrauterine pregnancy, with multiple neurofibromas developing on the patient's abdomen, back, and breasts. During the course of the pregnancy, three of the largest tumors were removed by electrocautery.

Past history at this time revealed that the patient had the usual childhood diseases, and an appendectomy at the age of 21 years.

Family history showed that the patient's father had died of a "heart attack." However, the patient's mother and two sisters were living and well. There was no known familial tendency to neurofibromatosis.

Laboratory findings during the two pregnancies were all within normal limits, although the patient was found to be Rh negative.

The second pregnancy progressed uneventfully, and the patient delivered a normal male child on Oct. 31, 1950.

The postpartum examination 6 weeks later showed normal involuted pelvic organs, but the cervix contained multiple small nodules 2 to 4 mm. in diameter, one of which was removed by punch biopsy.

Hematoxylin and eosin stains of the tissue revealed cervical tissue lined in part by stratified squamous epithelium, and in part by single columnar epithelium showing minimal lymphocytic infiltration. Within the stroma there was a benign neoplasm composed of interlacing strands of fibrous tissue and proliferative Schwann cells with a tendency to whorl formation. The lesion was well circumscribed but not encapsulated (Fig. 1). Bielschowsky silver stains of the tissue showed typical dark-staining axones running through the tumor (Fig. 2). The diagnosis neurofibroma of the cervix was made.

ABORTION OF DECIDUAL CAST COMPLICATING PREGNANCY IN UTERUS DIDELPHYS

MATHIAS F. F. KOHL, M.D., PH.D., ROCKFORD, ILL.

(From the Obstetrical Section, Swedish American Hospital)

SINCE Miller summarized the obstetrical literature on the clinical aspects of uterus didelphys in 1922¹ there have been no contributions of significance other than further affirmation of the conclusions obtained from the review of existing literature at that time. Miller pointed out that fertility and frequency of conception are not particularly affected but that abortion and premature labor are common complications. Labor is not infrequently associated with uterine inertia. Incarceration of the enlarged nongravid companion uterus and the consequent soft tissue pelvic dystocia necessitate delivery by cesarean section in many cases. The third stage of labor is complicated by increased blood loss due to the nonpregnant companion uterus acting like a full bladder in preventing normal postpartum contraction of the gravid uterus. Retention of lochia is also common due to malposition of the puerperal uterus as a result of its obstructing companion.

The case presented here is the account of three pregnancies in the same patient, two of which were under the supervision of the author, and is reported because of the problem arising from the decidual reaction occurring in the nongravid companion of the pregnant uterus. The literature on uterus didelphys in pregnancy gives little notice to the changes occurring in the nongravid companion other than statements regarding its enlargement and role in producing dystocia.

Mrs. J. S., a 30-year-old, para ii, gravida iii. Was first pregnant in 1939 at the age of 19 years. The anomaly of a double vagina, double cervix, and double uterus was not recognized at the initial prenatal visit because of limited examination. At approximately 4 months' gestation the patient was hospitalized after two days of scant bleeding. Just prior to admission there had been a sudden loss of bloody fluid. Bleeding and mild cramps continued in the hospital. On the third day of hospitalization the patient passed a mass of tissue per vaginam which she was told was the size of a six weeks' pregnancy. On the following day she was examined under gas anesthesia and was found to have a uterus didelphys. Quoting from the surgeon's operative note: "There was a double vagina with a thick septum separating the two vaginas. A double uterus with pregnancy being on right side, the bag of waters had previously broken. Cervix was 2/3 dilated and patulous. Operation—mild dilatation of the cervix, lower uterine segment packed with gauze." The cervical pack was removed 24 hours later. Bleeding continued and three days following the initial packing of the cervix the patient was again returned to surgery. The consultant's operative note is as follows: "The segment separating the two vaginas was excised, cervix was dilated, bag on one side ruptured, lower uterine segments of both uteri packed with gauze." Twenty-four hours later the packs were removed, which was followed immediately by the expulsion of the placenta and fetus. The fetus was estimated at four months' gestation and lived for a few hours. Pathologic descriptions of the tissue passed prior to the surgical induction of abortion and the placenta and fetus passed at the time of abortion were not recorded.

Upon recovery from the abortion the patient had hysterosalpingograms done and was advised, in view of the potential complications of pregnancy resulting from her condition, not to attempt to have another pregnancy. In 1947 the patient consulted a gynecolo-

gist concerning her chances of having a successful pregnancy. The left uterus was found to be $1\frac{1}{2}$ times larger than the right uterus, which was normal in size, and the opinion was expressed that the previous pregnancy had been in the left uterus. The possible complications of pregnancy were mentioned and pregnancy advised.

The patient was first seen by the author for prenatal examination on Nov. 20, 1947. The last menstrual period had been Sept. 29, 1947, with estimated date of confinement of July 6, 1948. The introitus was marital. The vagina contained a large redundant vaginal septum hanging from the anterior wall extending from under the urethra in midline to the anterior fornix between two separate cervices. The left cervix was larger than the right, both being healthy, soft, and closed. Two distinct uteri could be felt side by side, the right being slightly enlarged and the left $1\frac{1}{2}$ times enlarged. Both were softened. Contour was normal. Adnexa were not palpable. Pelvic measurements were gynecoid in type. On Jan. 5, 1948, both cervices were softened and showed a positive Chadwick sign. The right uterus was about the size, shape, and consistency of a three months' pregnancy and left uterus that of a two months' pregnancy. A Hegar sign was elicited in the right uterus. Quickening was experienced on the right side on Feb. 15, 1948. X-ray on June 8, 1948, revealed a frank breech presenting in right sacrotransverse estimated at thirty-six weeks' gestation with the presenting part floating. On June 24, 1948, vaginal examination revealed the right cervix displaced anteriorly high under the symphysis with the cervix partially effaced and patulous. The left cervix had rotated posteriorly behind the right cervix and was long and closed. The pelvis and hollow of the sacrum were filled by the left uterine mass the size of a small grapefruit. This mass could not be displaced. On July 1, 1948, under spinal anesthesia cesarean section was done. The right pregnant uterus lay anteriorly in midline while the left uterus lay posteriorly in the hollow of the sacrum. The bladder reflection onto the uteri contained large tortuous vessels. A lower uterine segment was not demonstrable. The relation of the cervix to the uterus resembled that of the neck on a gallon vinegar jug. The cervix was small with abrupt transition into the uterine corpus. A classical incision was done in the right uterus and a living 6 pound, 4 ounce female infant presenting as a frank breech in right sacrotransverse was extracted. The contracted uterus was displaced to the right and the left uterus was then elevated from the cul-de-sac with some difficulty because of the impaction. The left uterus was the size of a small grapefruit. The two cervices were completely separated and joined by a fibrous band indicating a complete separation of the Müllerian system. The bladder was reflected over both cervices. The lower uterine segment of the pregnant uterus was nonexistent. A fold of peritoneum ran between the cervices from the bladder reflection to the anterior surface of the rectum, the so-called vesicorectal fold. Each uterus had a single tube and ovary. The ovaries were normal and the right ovary contained the corpus luteum of pregnancy. The postpartum course was complicated by a temperature spike to 103° F. on the seventh postpartum day. Lochia serosa was scant and had a foul odor. The patient was given procaine penicillin G, 300,000 units daily for four days, and the temperature remained normal. The patient was discharged on the eleventh postpartum day. Postpartum examination on Aug. 3, 1948, revealed both cervices closed and healthy. The uteri were both slightly enlarged, side by side, anteriorly in the pelvis. The adnexa were negative. Examination on Sept. 3, 1948, revealed the uteri well involuted. On Nov. 28, 1948, the redundant anterior vaginal septum was removed under local anesthesia.

Mrs. S. presented herself for the third pregnancy on May 6, 1950, at age 30 years. Her last menstrual period had been Feb. 25, 1950, and estimated date of confinement was Dec. 4, 1951. She stated that she had had scant brownish discharge for three days at the time of her first and second missed menstrual periods. Pelvic examination revealed both cervices large, soft, and healthy. The right uterus was slightly enlarged and softened. The left uterus was the size, shape, and consistency of a ten weeks' pregnancy and was moderately tender. The adnexa were not felt. On May 8, 1950, the patient reported a scant brownish discharge which persisted for twenty-four hours. The stilbestrol routine of Smith and Smith² was instituted with initial dosage of 15 mg. stilbestrol daily. Buccal progesterone, 30 mg. daily, was also prescribed. On May 19, 1950, the patient again reported

scant spotting. The left uterus was now five fingerbreadths above the symphysis in the left lower quadrant. Speculum examination showed scant brownish discharge coming from the left os (gravid uterus). This discharge continued for three days and then subsided. On June 11, 1950, the patient again reported scant bleeding. The fundus was now in the midline extending to two fingerbreadths below the umbilicus. There was marked rotation of the two uteri. Speculum examination showed a brownish serosanguineous discharge coming from the right cervix (nongravid uterus) which had rotated posteriorly. The patient was placed at bed rest. A mild sedative was prescribed. Stilbestrol was increased to 25 mg. per day and buccal progesterone was continued at 30 mg. daily. On June 13, 1950, the patient had mild cramps and passed a decidua 6 cm. in length and 3.5 cm. in diameter. The patient continued to have a serosanguineous discharge until June 22, 1950, at which time she was allowed out of bed. Cramping and pelvic heaviness had disappeared and only a slight brownish residual discharge persisted, coming from the right cervix. The patient was continued throughout her pregnancy on stilbestrol according to the schedule of Smith and Smith. On Nov. 8, 1950, pelvic examination revealed the situation similar to that found in the previous pregnancy with the nonpregnant uterus the size of a grapefruit incarcerated in the hollow of the sacrum with the pregnant uterus rotated anteriorly. A small fetus was presenting in vertex left occipitoanterior with the head high above the pelvic brim. On Nov. 20, 1950, under cyclopropane anesthesia cesarean section was done. Pelvic findings were identical to those of the previous pregnancy except for the pregnancy and corpus luteum of pregnancy now being in the opposite side. There was no demonstrable lower cervical segment and a classical incision was made with delivery of a viable 6 pound, 4 ounce female presenting in vertex left occipitoanterior. Sterilization by cornual resection and partial salpingectomy was done. The patient was afebrile except for a temperature rise to 100° F. on the third postoperative day. The patient was discharged on the ninth postoperative day. Lochial drainage was profuse. Postpartum checkup on Dec. 8, 1950, showed both uteri side by side in the pelvis. The right uterus was slightly enlarged. The left uterus was the size of a small grapefruit and tender. The patient was just concluding a normal menstrual cycle. On Jan. 11, 1951, both uteri were well involuted. The cervixes were closed and healthy.

Summary.—This case has been presented to point out the complications during pregnancy which may arise as the result of the decidua reaction in the nongravid companion uterus of uterus didelphys. There is striking similarity between the patient's first and third pregnancies and the differences in management and outcome furnish much material for speculation. Since abortion of the decidua of the companion nongravid uterus in uterus didelphys has been shown to be an accomplished fact, it becomes necessary therefore in the management of bleeding in uterus didelphys to determine (1) which uterus contains the pregnancy and (2) which uterus is doing the bleeding. This can be accomplished only by adequate abdominal and pelvic examination of the uteri supplemented by speculum examination of the cervixes. Only in this manner can rational therapy for the bleeding be instituted and a prognosis for outcome of the pregnancy be determined.

References

1. Miller, N. F.: *AM. J. OBST. & GYNEC.* 4: 398, 1922.
2. Smith, O. W., and Smith, G. V.: *AM. J. OBST. & GYNEC.* 58: 944, 1949.

CANFIELD CLINIC, EMPIRE BUILDING

MULTIPLE NEOPLASMS OF THE OVARIES ASSOCIATED WITH CARCINOID OF THE APPENDIX

ISAAK GRUNSTEIN, M.D., AND DAVID NYE BARROWS, M.D., F.A.C.S.,
NEW YORK, N. Y.

*(From the Department of Gynecology of the New York Polyclinic Medical School
and Hospital)*

MUCH has been written about multiple tumors of the ovary, but little about ovarian and appendiceal tumors existing concomitantly. The finding of a carcinoid of the appendix, with a Brenner tumor of one ovary, and a pseudomucinous cystadenoma and fibroma of the second ovary, all in one patient, seemed unusual and, therefore, worthy of being reported.

E. B. (Adm. No. 3010/1950), 53-year-old white married woman, appeared for examination on April 5, 1950, because of slight lower abdominal pain, abdominal distention, and shortness of breath of three weeks' duration.

Her family history revealed that her father died at the age of 63 years of carcinoma of the kidney. Her mother died at the age of 54 of diabetes. There is a history that several members of her family were hard of hearing.

The patient's past history revealed she had had scarlet fever twice, measles, chicken pox, and otitis media. Menses began at the age of 10 years, with a regular 28-day cycle, of 5 days' duration, with moderate bleeding and no pain. She married at the age of 25 years and had several pregnancies that terminated in spontaneous abortions. Her menstrual periods ceased three years ago with no untoward menopausal symptoms since that time. For the past two years, she has been hard of hearing due to otosclerosis. Her history was otherwise noncontributory.

Her general examination was unremarkable. Heart and lungs showed no pathological changes. Liver, spleen, and kidneys were not enlarged or tender. Blood pressure was 170/90, weight 134 pounds, height 5 feet, 4 inches.

Abdominal examination revealed a nontender, firm, nodular mass, arising in the pelvis and extending to the level of the umbilicus. Pelvic examination showed a parous introitus, a small cervix, not lacerated or eroded, with no bleeding. Intimately attached to the cervix was a large, firm, nodular mass which arose from the pelvis as described above. The adnexa could not be palpated separately.

The clinical impression at that time was multiple fibromyomas of the uterus.

The urine was negative for albumin and sugar. Hemoglobin was 78 per cent, red blood cells 4,010,000. The white blood count was 8,700, with 71 per cent polymorphonuclear leucocytes. Sedimentation rate was 40 mm. per hour (Westergren). The Wassermann test was negative and the fasting blood sugar 92 mg. per cent (Folin-Wu).

Under general anesthesia, a laparotomy was performed on April 20, 1950. The following are the operative findings:

There was a large, cystic, nodular mass filling the pelvis and extending up to the umbilicus, partly adherent to the parietal peritoneum and densely adherent to the tissues in the true pelvis. This mass originated in the left ovary. The uterus was small, displaced anteriorly by the large mass. The right ovary and tube were involved in the adhesions. The right ovary was the size of a walnut and stony hard in consistency. Adhesions from the right adnexa extended upward to the right pelvic wall, enveloping part of the cecum and appendix. The appendix pointed downward and was attached to the adhesions of the anteromedial surface of the intestinal wall in the pelvis, the region where the previously mentioned large cystic mass had been embedded. At the distal end, the appendix showed a bulbous swelling, suggesting the diagnosis of carcinoid.

Due to extensive adhesions, a supracervical hysterectomy and bilateral salpingo-oophorectomy and appendectomy were performed.

The postoperative course was uneventful and the patient left the hospital fully recovered, and in good condition.

Follow-up examination on Dec. 20, 1950, showed the patient to be in good health, and asymptomatic; however, the sedimentation rate was still elevated (18 mm. per hour).

Additional follow-up examination of Jan. 6, 1951, revealed that the patient had no complaints. She had gained seven pounds and the sedimentation rate had returned to normal. The pelvic examination at this time showed the cervix to be freely movable with no pain or induration. There was no adnexal or parametrial thickening or induration. High up in the region of the right pelvic wall was a sensation of resistance, suggesting the presence of adhesions in the area where the peritoneum was separated in removing the embedded appendix.

Examination on May 7, 1951, showed the patient to be in good general condition with no abdominal or vaginal infiltrations or masses. Also, her previously elevated blood pressure had dropped to the normal levels of 120/80.



Fig. 1.—*a*, Multiloculated pseudomucinous cystadenoma. *b*, Fibroma. *c*, Brenner tumor. *d*, Uterus. *e*, Carcinoid of the appendix.

Pathologic Report (No. 60290, April 20, 1950).—

"Specimen consists of a uterus with the right tube and ovary attached. Separately, there is the appendix and one large ovarian cyst to which is attached a fallopian tube. The uterus measures $5 \times 4.5 \times 2$ cm. The endometrium is pink and measures less than 1 mm. in thickness. The myometrium measures 2 cm. in thickness, the serosa is grayish-brown and smooth.

"The right tube measures $7\frac{1}{2}$ cm. in length, the wall is thickened and it is adherent to the ovary by thin adhesions. The attached right ovary measures 2.5 cm. in diameter, the cut surface reveals a well-defined tumor nodule, 2 cm. in diameter, the cut surface of which is firm and grayish-white in color.

"The left tube is similar in appearance to the right; it is bound down to an ovarian mass, measuring 15 cm. in diameter. The cut surface of the mass reveals multiple locu-

lated cavities filled with mucoid material. There are patchy areas of hemorrhage and necrosis. At one edge of this tumor mass there is a dense, fibrous nodule, 2 cm. in diameter, similar in appearance to the one described in the right ovary.

"Microscopic examination reveals a uterus in which the endometrium is cystic in type, the myometrium reveals some atrophy, the Fallopian tubes are unremarkable except for a few adhesions.

"In the left ovary, there are multiloculated cysts lined by columnar, globular, mucin-producing epithelium. The tumor nodule at one edge of the cyst consists of dense whorls of fibrillary connective tissue. The nuclei of the fibroblasts are large, oval and the cytoplasm is homogeneous and pale in color. There is pseudoencapsulation formed by the dense packing of the fibrous connective tissue. Diagnosis: Pseudomucinous cystadenoma and fibroma of left ovary.

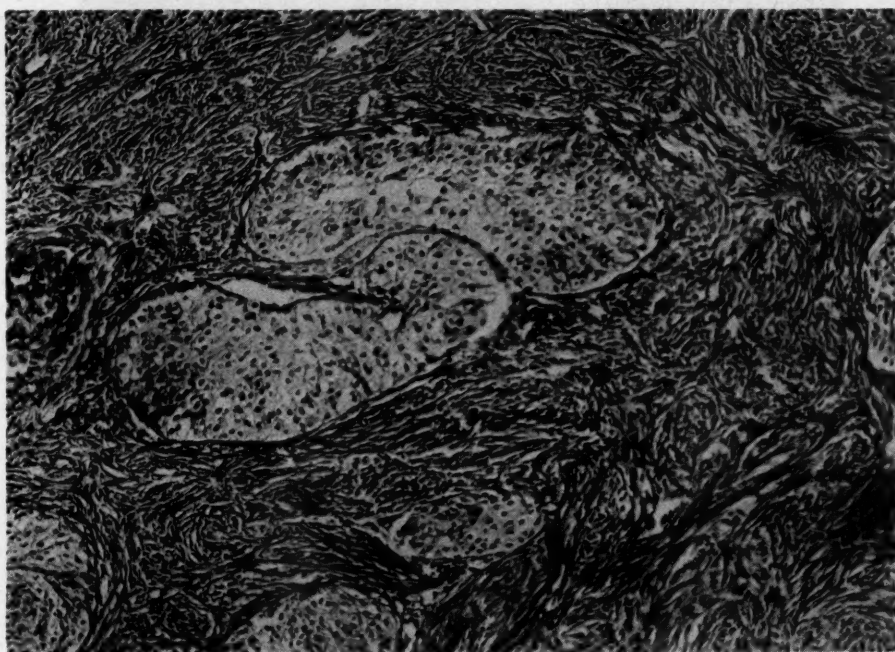


Fig. 2.—Brenner tumor: island of epithelial cells showing the tendency toward acinus arrangement. The islands are surrounded by dense fibrous tissue. ($\times 200$.)

"In the right ovary, the tumor is composed of fibrillary connective tissue in which are embedded numerous clusters of cells that are polyhedral in shape and resemble squamous epithelium. The nests are largely oval in shape and approximately 1-2 in number per low-power field. Some of the nests of cells had central cystic areas and the cells lining the cysts were columnar in type. The cystic portion in some contained a pale blue mucoid material. Under higher power the nuclei were oval in shape and the cytoplasm homogeneous and pale. No mitotic figures were seen. This was diagnosed as a Brenner tumor.

"In the appendix, there is a tumor arising from the mucosa consisting of strands and clusters of small, round cells that infiltrate the muscularis and serosa. The nuclei of the cells are spherical or oval in shape and the cytoplasm scanty. These cells are polyhedral and resemble those seen in the islands of epithelial cells within the Brenner tumor.

"*Diagnosis:* Cystic endometrium, atrophy of myometrium, pseudomucinous cystadenoma and fibroma of left ovary, Brenner tumor of right ovary, and infiltrating carcinoid of the appendix."

Comment.—The relationship between pseudomucinous cystadenoma and Brenner tumor is discussed by Foot¹ and described by Danforth, who could demonstrate structures in his case (pseudomucinous cystadenoma) resembling the Walthard cell nests of the Brenner tumor with columnar cells palisading about a differentiated core of fusiform cells, which may indicate a relationship between pseudomucinous cystadenoma and Brenner tumor.

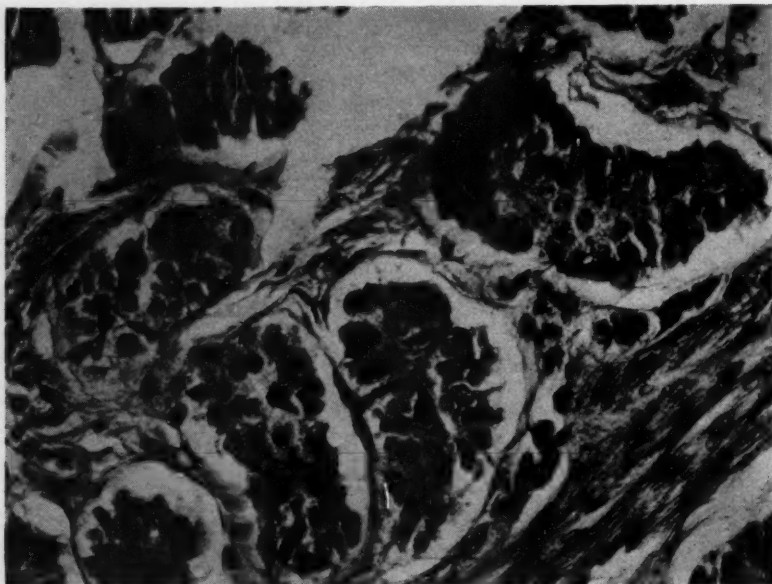


Fig. 3.—High-power magnification of the carcinoid of the appendix showing islands of epithelial cells surrounded by dense fibrous tissue. ($\times 400$.)

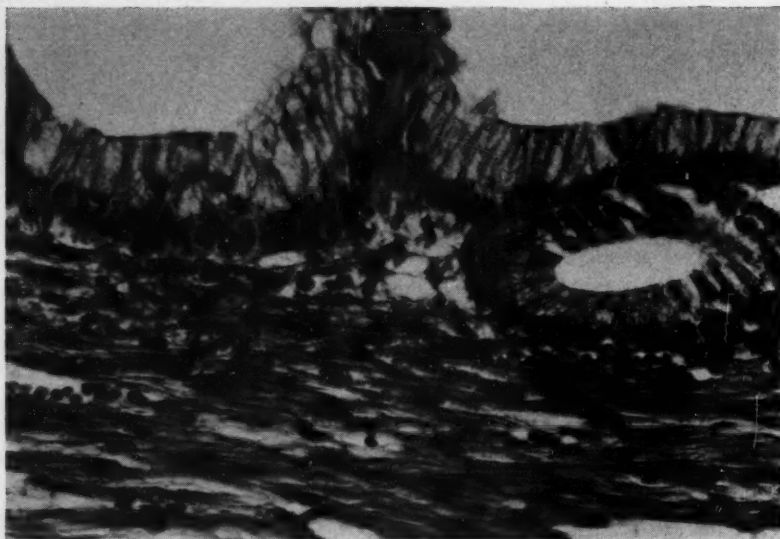


Fig. 4.—Pseudomucinous cystadenoma. (High power.)

It is well known that pseudomucinous cystadenomas may rupture spontaneously or during operative procedure, with a resulting seeding out of daughter cells into the peritoneum leading to a condition known as pseudomyxoma peritonei.

Regan,² Jondahl and co-workers, as well as many other authors, have emphasized the benign nature of the Brenner tumor. However, Dubrausky, Massenbach,³ and Von Numers⁴ have reported cases of Brenner tumor in which malignancy was also present.

Fibroma of the ovary is commonly associated with pseudomucinous cystadenoma and according to R. Meyer^{5, 6} fibromas of the ovary may have their origin in Brenner tumor.

The association of a carcinoid of the appendix in this case greatly adds to its interest. Frankl, as quoted by Novak⁷ in his textbook, has referred to the Brenner tumor as the carcinoid of the ovary. Though this may be a poor term, there are certain features in common between Brenner tumor of the ovary and the carcinoid of the appendix, mainly the distribution of the nests of cells and the similar polyhedral squamouslike nature of the cells. Pearson and Fitzgerald⁸ reviewed 140 cases of carcinoid of the appendix. They observed that appendiceal carcinoid rarely showed metastases and that those of other areas may be very slow growing. They make the statement that all carcinoid tumors, other than those found in the appendix, should be considered malignant. In their series of 140 cases, 23 per cent also showed a second malignant tumor of noncarcinoid type.

From the above discussion, it might be well to assume a more guarded outlook for patients with tissues containing multiple neoplastic changes. The only impression that can be drawn from the combination of tumors present in this patient is that, perhaps, her tissues are rather susceptible to neoplastic changes.

The immediate prognosis in this case seems good, the future prognosis may well be guided by the inferences stated above.

Summary.—A case is reported of multiple neoplasms of the ovary, consisting of pseudomucinous cystadenoma, Brenner tumor, and fibroma, associated with a carcinoid of the appendix.

Grateful acknowledgment is given to Dr. S. A. Gladstone, Pathologist, and Dr. A. U. Blausetin, Associate Pathologist of the New York Polyclinic Medical School and Hospital for the preparation and description of the specimens.

References

1. Foot, N. C.: *Pathology in Surgery*, Philadelphia, 1945, J. B. Lippincott Company.
2. Reagan, J. W.: *AM. J. OBST. & GYNEC.* 60: 1315, 1950.
3. Dubrausky, V., and Massenbach, M. V.: *Zentralbl. f. Gynäk.* 69: 370, 1947.
4. Von Numers, Claës: *Acta obst. et gynec. Scandinav.* (Suppl. 2) 25: 114, 1945.
5. Meyer, Robert: *Arch. f. Gynäk.* 148: 541, 1932.
6. Meyer, Robert: *Zentralbl. f. Gynäk.* 56: 770, 1932.
7. Novak, Emil: *Gynecological and Obstetrical Pathology*, ed. 2, Philadelphia, 1947, W. B. Saunders Company.
8. Pearson, Carl M., and Fitzgerald, Patrick J.: *Cancer* 2: 1005, 1949.

INTERSTITIAL PREGNANCY DEVELOPING INTO THE BROAD LIGAMENT

ALFRED J. KOBAK, M.S., M.D., AND LAWRENCE LE VINE, M.D., CHICAGO, ILL.

(From the Department of Obstetrics and Gynecology, Mount Sinai Hospital; and the University of Illinois, College of Medicine)

ALTHOUGH interstitial pregnancy is an infrequent form of tubal pregnancy, there are sufficient cases on record to make isolated case reports unnecessary when only typical findings are demonstrable. These pregnancies are most frequently characterized by an elevation of the affected cornu, displacement of the fundus toward the opposite side, and insertion of an intact tube into the inferior surface of the enlargement. These findings are known as the Ruge-Simon syndrome.¹ When this syndrome is present it has been found that the implantation most frequently occurs in the mid-area of the interstitial portion of the tube, and it is then known as a "true interstitial pregnancy."^{1,2} Less frequently the distal third of the interstitial portion of the tube, adjacent to the isthmus, may be the site of the trophoblastic implantation. This is known as a "tubo-interstitial pregnancy"^{1,2} which might rupture earlier than the former because there is less uterine muscle tissue surrounding the ovisac. The upward direction of growth of an interstitial pregnancy usually brings about the above-described Ruge-Simon picture with eventual perforation and intraperitoneal rupture. The latter more frequently occurs after the third month of gestation. However, both Wynne² and Ash¹ mention the rare occurrence of rupture of the gestational sac between the leaves of the broad ligament when the tubo-interstitial portion of the oviduct is involved. The following case represents an interstitial pregnancy with development of an unruptured ovisac between the leaves of the broad ligament.

D. M., a 30-year-old white woman, pregnant for the first time, was admitted to the Mount Sinai Hospital on Oct. 9, 1949. She had her last normal menstrual period three months prior to admission. When she missed her first menstrual period, a Friedman test was reported negative. A few weeks later she developed attacks of nausea and spotting, and colostrum was noted. She was, therefore, treated as having a threatened abortion. The patient apparently responded to treatment until two days prior to admission when the vaginal spotting became more active and a feeling of vertigo developed.

On admission, the pulse and blood pressure were within normal limits. The abdomen was soft with some tenderness in the left lower quadrant but no rebound tenderness. Pelvic examination revealed the cervix to be softened, the uterus slightly enlarged, and a tender mass about the size of a golf ball in the region of the left cornu. The blood study revealed a red count of 3.7 million, a white count of 10,000, and hemoglobin of 11.7 Gm. The diagnoses entertained at this time were ectopic pregnancy, incomplete abortion, or missed abortion. A diagnostic curettage was performed, and it revealed an early proliferative-phase endometrium with a limited area of decidual reaction, but no trophoblastic tissue.

Six days later the mass was felt to be much larger and in the region of the ovary. A laparotomy was then performed with the diagnosis of an unruptured ectopic pregnancy, probably ovarian. The enlargement noted on pelvic examination was a mass that was attached to the upper left uterine border, protruding between the leaves of the broad ligament. In order to remove this tumor it was necessary to first make an incision into the broad ligament between the round ligament and left tube (Fig. 1). It was found to originate from the interstitial portion of the left tube and was enucleated by wedged

incisions. The gestational mass was continuous with the left oviduct and both were removed. The opened specimen revealed a cystic cavity and an embryo 15 mm. in size (Fig. 2). The cystic cavity was surrounded by a fasciculated structure varying from 1

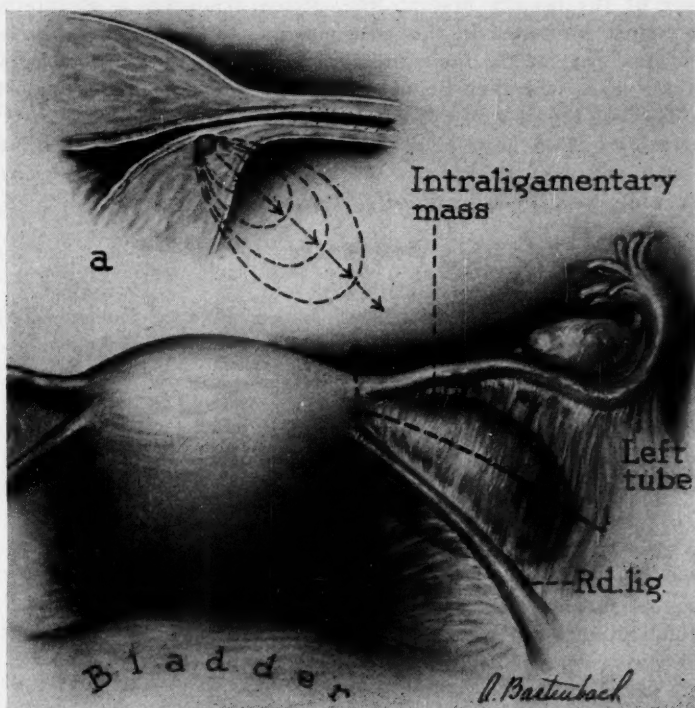


Fig. 1.—Diagrammatic reconstruction of pelvic picture. Insert *a*, authors' impression: manner of development of ovum into the broad ligament. (1) Line of incision into broad ligament. (2) Site of wedged enucleation into cornu proper.



Fig. 2.—Opened specimen showing embryo.

to 6 mm. in thickness, which is characteristic of myometrium. Microscopic examination shows that the cyst wall was lined by cuboidal ciliated epithelial cells characteristic of those found in the oviduct. The lack of endometrium in the cyst cavity excludes saccululation of the uterus.

The absence of the usually present Ruge-Simon syndrome is of interest. It is our belief that the picture presented in this case was due to the implantation of the trophoblast into the inferior part of the tubointerstitial portion of the tube. Progressive enlargement of the ectopic mass was then between the leaves of the broad ligament instead of upward. (See inset *a*, Fig. 1.) It is further interesting to speculate that uninterrupted growth of this embryo could have ultimately resulted in an intraligamentary pregnancy. We, therefore, offer this case as evidence that an interstitial pregnancy may occasionally develop into the rarely seen broad ligament gestation.

References

1. Ash, J. E.: Surg., Gynec. & Obst. 54: 930, 1932.
2. Wynne, H. M. N.: Am. J. Surg. 7: 382, 1929.

25 EAST WASHINGTON STREET

GUNSHOT WOUND OF THE GRAVID UTERUS

Report of a Case

WAYNE N. JACOBUS, M.D., DETROIT, MICH.

(From the Department of Obstetrics and Gynecology, Wayne University College of Medicine, and the Gynecology Service, Detroit Receiving Hospital)

PENETRATING wound of the gravid uterus by passage of a missile through the abdomen is uncommon. Reports of such cases are meager and to our knowledge only four cases are reported^{1, 2, 3, 4} in the English literature. The following case is presented not only because of the rarity of the occurrence but also because of the fact that the patient carried the pregnancy for eight days following the receipt of the wound.

Mrs. H. M. (DRH No. 50-11908), a 23-year-old white woman, gravida ii, para i, was admitted to the Detroit Receiving Hospital at 8:30 P.M. on Aug. 26, 1950, thirty minutes after she had been struck in the abdomen by a bullet fired during an attempted robbery. The patient gave a history of being four and one-half months pregnant. Her physical examination was essentially negative except for a puncture wound in the right lower quadrant at McBurney's point, minimal lower abdominal tenderness, and a subcutaneous mass in the left buttock. Intravenous fluids were administered and a Levine tube inserted. Her hemoglobin was 10.5 Gm. Examination of a voided specimen of urine was negative except for the presence of occasional white and red blood cells in several high-power fields. The uterus could be palpated abdominally and seemed to be the size of a 16 to 20 weeks' pregnancy. There was no bleeding from the vagina or rectum.

Because of the location of the wound of entrance, an intravenous pyelogram was taken. It revealed no extravasation of dye nor any distortion of any part of the urinary tract. A flat plate of the abdomen showed the presence of a metallic slug overlying the head and neck of the left femur. There was no pelvic bone injury nor evidence of free air beneath either diaphragm.

A retrograde cystoscopic examination also failed to reveal any urinary tract injury. Under spinal anesthesia a laparotomy was performed and a large amount of fresh blood was found in the peritoneal cavity. The uterus was enlarged, soft, and loosely fluctuant, and contained an apparently normal pregnancy of about 16 to 18 calendar weeks' development. The point of entrance of the bullet into the uterus was identified by a wound 1.5 cm. in diameter situated immediately posterior to the cornual end of the right tube (Fig. 1). Bleeding from this point was controlled by interrupted sutures of No. 60 cotton, placed so as to close both muscularis and serosal layers. The wound of exit from the uterus measured 2 cm. in diameter and was located just above the attachment of the left uterosacral ligament. There was moderate bleeding from this wound but there was no evidence of escape of amniotic fluid. This wound likewise was closed and hemostasis obtained with interrupted sutures of No. 60 cotton. The point of exit from the peritoneal cavity was found just to the left of the rectosigmoid in the cul-de-sac of Douglas, and, as there was no hemorrhage from this point and no injury to the rectum, this wound was not closed. In addition to the uterine injuries there were four perforating wounds of the terminal ileum, each of which was closed with interrupted No. 60 cotton sutures. Fetal movements were noted immediately prior to the closure of the incision. The abdominal incision was closed in layers in the routine manner, a continuous suture of No. 00 chromic gut being used in the peritoneum, and single interrupted sutures of cotton approximating the fascia and the skin.

The patient returned to the ward in good condition and was given 500 c.c. of whole blood. The Levine tube was replaced by an Honor-Smathers long intestinal decompression tube. Six hours following laparotomy the fetal heart sounds could not be heard nor movements felt, but this is not surprising in view of the presence of a postoperative bandage and a firmly splinted lower abdomen. On the first postoperative day the patient's temperature was 101.6° F. and there was minimal abdominal distention. Antibiotic therapy consisting of a daily dose of 300,000 Oxford units of repository penicillin plus a daily dose of 1.0 Gm. of

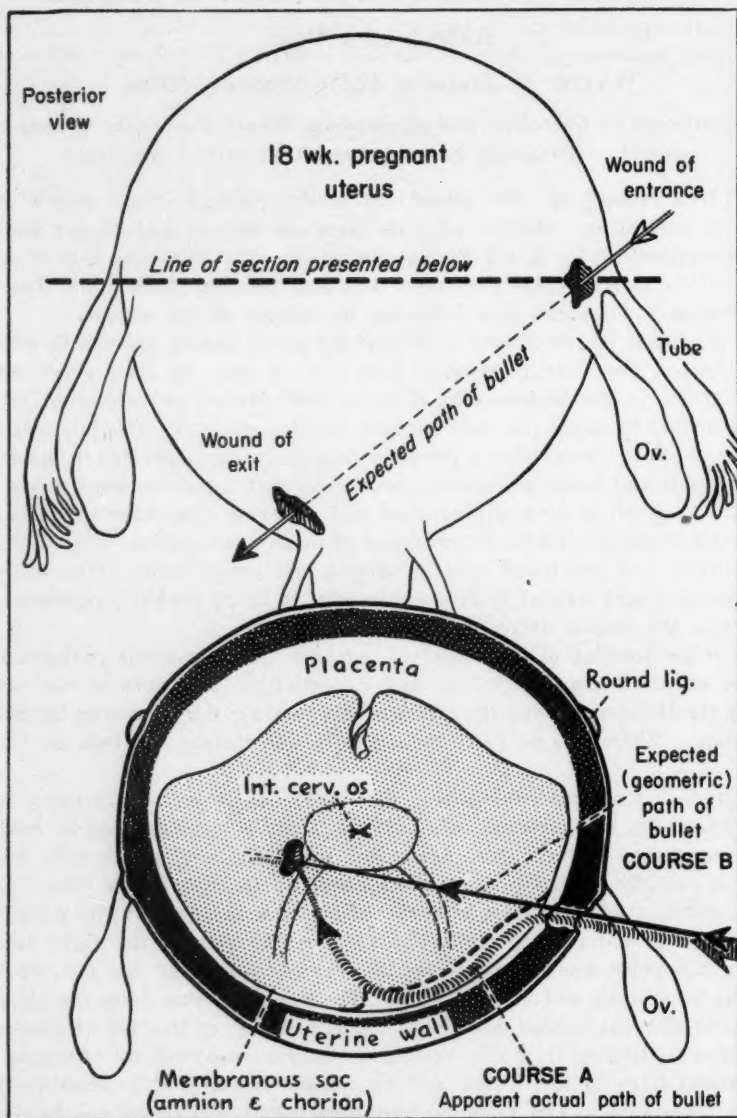


Fig. 1.

streptomycin was begun. Her fever continued through the second postoperative day during which she complained of incisional pain and cramps and burning on urination. A catheterized urine specimen revealed many bacteria but only occasional leucocytes. The patient had two normal bowel movements on this day.

In view of x-ray evidence of peritonitis, ileus, and the possibility of small bowel obstruction, the long intestinal drainage tube, on the third postoperative day, was passed beyond the ligament of Treitz with the aid of the fluoroscope. Her condition improved rapidly thereafter and the tube was removed on the fourth postoperative day. The skin sutures were removed on the fifth postoperative day, at which time the incision was found to be healing per primam.

On the evening of September 2 (7 days following operation) the patient began to have a bloody vaginal discharge without discernible uterine contractions. The bleeding subsided the following day but she then began to have intermittent lower abdominal cramps and at 6:20 P.M. on September 3, eight days after the injury, she spontaneously delivered a macerated male fetus of approximately 19 calendar weeks' development. The placenta was expressed intact shortly afterward and 1 c.c. of Pitocin was administered intramuscularly. The estimated blood loss was 50 c.c.

The patient's postpartum course was uneventful except for a single rise in temperature to 100.4° F. on the fifth postpartum day. She was discharged on the eighth postpartum day. A subsequent visit to the clinic six weeks post partum showed good uterine involution and normal pelvic findings.

Examination of the placenta after delivery revealed several interesting points. The implantation site was apparently low on the anterior wall, judging from the location of the rent of fetal exit from the amniotic sac, and thorough examination of the placenta failed to reveal any evidence of trauma such as would have been caused by a bullet. There likewise was no evidence of the bullet's having pierced the amniotic sac. Positive pathologic findings in the placenta consisted of a small area of red infarction and two small recent noncommunicating lacerations on the maternal surface; there were also some gelatinous, blood-stained thickenings of the membranes which may have represented trauma resulting from the passage of the bullet across the posterior aspect of the amniotic sac without perforating it. The fetus showed no evidence of trauma from the bullet.

Summary.—A case in which a bullet traversed an 18 weeks pregnant uterus without visibly damaging its contents is presented. The injury to the uterine wall, consisting of holes of entrance and exit, was sufficient, however, eventually to cause fetal death in utero and resultant subsequent delivery of the macerated fetus. In addition, there were multiple perforations of the lower ileum, which were closed; mild postoperative peritonitis and ileus occurred. Under antibiotic therapy and continuous intestinal drainage, the patient recovered quickly and was discharge from the hospital 16 days following the emergency laparotomy and 8 days following her delivery.

Comment.—The passage of a bullet through the wall of a pregnant uterus is usually followed by intrauterine and intra-abdominal hemorrhage, death of the fetus, and premature onset of labor. The rent in the uterus can usually be repaired without difficulty, and thus hysterectomy, with its forfeiture of future childbearing potential, is seldom necessary.

The fact that the bullet in this case could enter the 18 weeks pregnant uterus just posterior to the right cornu and leave it immediately above the attachment of the left sacro-iliac ligament means that the bullet *had* to traverse a portion of the uterine cavity. The fact that it was able to do this without rupturing the amniotic sac must mean that it temporarily "creased," or indented the sac during its passage. This would have constituted quite an "underwater concussion" and is the most probable cause of the fetal death. It would appear that there was too little, if any, hemorrhage from the uterine wounds into the uterine cavity to have initiated labor immediately, and this did not occur until eight days later. The absence of old blood clots in the uterine contents at the time of its emptying speaks against any intrauterine hemorrhage. The small area of red infarction in the placenta undoubtedly was evidence of some localized clotting of maternal blood, and its age probably coincided with the passage of the bullet through the uterus. How long the fetus had been dead cannot be ascertained, but it is believed to have been longer than 72 hours prior to delivery.

Whether the course of this bullet through the uterus and around the amniotic sac was unusual, or an anticipated phenomenon, cannot be determined as, to the best of the author's knowledge, there have been no experimental studies on this subject. It seems strange that a projectile with sufficient velocity to penetrate the two walls of a uterus should be deflected by a thin amniotic membrane filled with fluid.

The apparent intrinsic tensile strength of the amnion-chorion sac in this case is nothing short of amazing.

The author wishes to express his appreciation of the help and encouragement given by Dr. Charles S. Stevenson, Professor of Obstetrics and Gynecology, and Miss Evelyn J. Erickson, head of the Medical Art Department, of Wayne University College of Medicine.

References

1. Holters, Otto R., and Daversa, Benjamin: AM. J. OBST. & GYNEC. 56: 985, 1948.
2. James, H. P., and Smythe, F. W., Jr.: Memphis M. J. 24: 131, 1949.
3. Belknap, R. E.: J. Maine M. A. 30: 13, 1939.
4. Belcher, C.: Brit. M. J. 1: 896, 1917.

1512 ST. ANTOINE STREET

MONOAMNIOTIC TWIN PREGNANCY: REPORT OF FIVE NEW CASES

JOHN A. KING, M.D., J. S. HERRING, M.D., E. D. WITT, M.D., AND
BEVERLY BLOOD, M.D., NEW ORLEANS, LA.

(From Touro Infirmary and The Sara Mayo Hospital)

THE most comprehensive recent report on this subject in the English literature was in 1935 by Quigley.¹ He reported 109 cases (including one of his own) from the world literature. The mortality rate for the viable babies was given by him as 68 per cent. The high fetal loss is almost entirely due to the knotting and entanglement of the two cords which occurred in about 58 per cent of the cases in his series. Congenital abnormalities such as developmental defects of the heart are relatively common.

The incidence of monoamniotic twins is stated to be one to 132 sets of twins or one monoamniotic pregnancy to about 16,000 deliveries (Ahlfeld as quoted by Béla²). However, we are certain that many monoamniotic twin cases are not recognized as such and reported. A careful examination of the relations of the cords and membranes should be made in all cases of twins. We are struck with the fact that our five cases of monoamniotic twins occurred in the City of New Orleans in a period of 18 months. In a review of 332 twin pregnancies at Chicago Lying-in Hospital for the period of 1931 to 1941, no monoamniotic twins were reported by Potter and Crunden.³

We report five cases of monoamniotic twin pregnancies observed since October, 1949. We are indebted to Drs. Edward Nelson, Walter Levy, and Katherine Havard for permission to include their cases. We have been able to gather 34 cases from the world literature, which, added to the 109 of Quigley, give a total of 148 cases. Quigley reported 17 double live births, and we add 21, of which both babies survived the neonatal period in 13 instances and one baby in 6 instances. Quigley reports 20 single live births to which we add 5, with 5 survivals. In two instances the survival was not stated. Total—37 surviving babies out of a possible 66 babies from 33 pregnancies of greater than 7 months' duration. There were in our collected series 6 abortions at from 5 to 6½ months and 6 double stillbirths. In this series there were 1 anencephalic, 2 babies with congenital heart disease, 1 of whom had situs inversus viscerum, and both babies of one set of twins had cleft palates and hare lips. One monstrosity consisting of an acardiac monster in the same sac with a normal 6 months' fetus was reported.

CASE 1.—Mrs. J. A. J., aged 35 years, was a primigravida whose last menstrual period was Jan. 4, 1949, and the expected date of delivery Oct. 11, 1949. The patient had an uneventful pregnancy, twins being suspected in July, and the diagnosis confirmed roentgenographically. The onset of labor was preceded by spontaneous rupture of the membranes at 5 P.M. on Oct. 1, 1949. Contractions began at 7 P.M., and full dilatation of the cervix was attained at 6:15 A.M. October 2. The first baby was in the right occipitoposterior position and was delivered by a Scanzoni midforceps maneuver at 6:26 A.M. Immediately

after delivery the knotted and twisted cords prolapsed, and the cord of the second twin was found to be pulseless. A rapid internal podalic version and breech extraction were performed, and the second baby was resuscitated with some difficulty, using a tracheal catheter and oxygen. Both babies were girls, the first weighing 5 pounds, 6 ounces, and the second 5 pounds, 9 ounces. They remained in oxygen for six hours, thereafter developed normally. They left the hospital with the mother on the seventh day. A description of the placenta by Dr. Harold Cummins, Professor of Anatomy at Tulane University, follows: "The placenta is oval in outline, length 20 cms., greatest breadth 17 cms., greatest thickness 3.6 cms. The two cords, which are attached eccentrically and in the narrower area of the ovoid, are separated at their attachments by an interval of 3 cms. The cords are entwined in several turns and at a distance of 28 cms. from the placenta they are tightly knotted together. In the fresh state, as in the preserved specimen, the cords when unwound maintained the spiral course impressed by their entwining; no attempt was made to untie the complex knot. The fetal surface of the amnion presents no sign of septal remains or any other indication that a membranous septum ever existed. There is nothing otherwise noteworthy about the fetal surface or the maternal surface." This placenta is shown in Fig. 1.

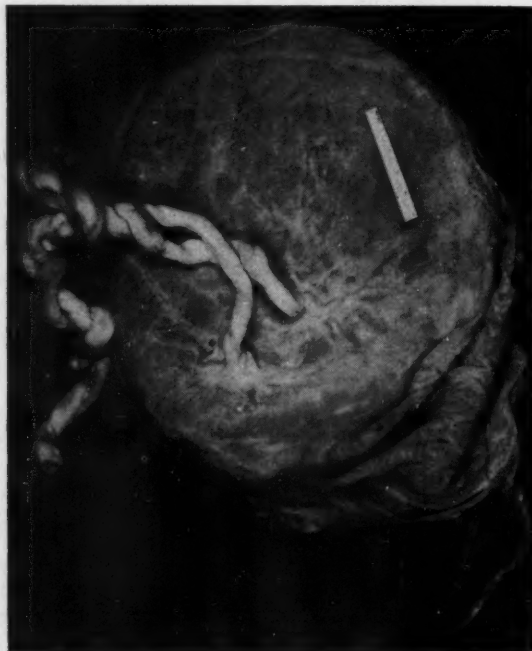


Fig. 1.

CASE 2.—Mrs. M. J. P. was also a primigravida, aged 30 years. Her last menstrual period was Feb. 11, 1950, and estimated date of delivery Nov. 18, 1950. The pregnancy was uneventful, twins being diagnosed by auscultation of the different heartbeats on Sept. 12, 1950. The patient went into labor on November 22, and after a tedious labor of 18 hours, the membranes were artificially ruptured at full dilatation, and the first baby was delivered from a brow presentation by flexing the head and a midforceps extraction. The second baby was delivered immediately by version and breech extraction. During the delivery of the body it was noted that the two cords were looped about each other. The first baby weighed 6 pounds, 8½ ounces, the second 6 pounds, 6 ounces. Both were girls and were in good condition. They went home with the mother on the seventh day and have remained healthy. A description of the placenta by Dr. Cummins follows: "Pla-

centa is oblong in outline, length 24 cms., greatest breadth 17 cms.; greatest thickness 2.7 cms. The two cords are attached near the center of the placenta, and are aligned with its long axis. The cord attachments are 3 cms. apart. There is less entwinement of the cords than in the above specimen; there is a loose transverse looping of one cord around the other at a level of 20 cms. from the placenta. The fetal surface of the amnion shows no indication of septal remains, the irregularity overlaid by the ruler is a regional lifting of the amnion from the chorionic plate." This placenta is seen in Fig. 2.

CASE 3.—Mrs. V. B. (patient of Dr. Edward Nelson) was aged 24 years and had had two previous pregnancies, one normal pregnancy and one early abortion. The last menstrual period began on April 21, 1950. The patient was treated for threatened abortion in June, and twins were diagnosed in November by auscultation, the diagnosis being confirmed by radiographic examination. The expected date of delivery was Jan. 31, 1951.



Fig. 2.

The patient was hospitalized on Dec. 8, 1950, for vaginal spotting. Hydramnion developed during this time. Labor started spontaneously on December 15, and was short. The first baby presented by vertex and was delivered by low forceps maneuver. The second baby was in a transverse lie and was delivered by version and extraction. The first baby was in considerable difficulty from birth. A tracheal catheter and oxygen were used for resuscitation, and intracardiac epinephrine was used for stimulation. This baby died in three hours. The second baby remained in good condition. Both were girls. An autopsy of the first baby revealed marked generalized edema, transudated fluids in pleural and peritoneal cavities, a picture very similar to that of hydrops fetalis. The brain was cystic, the ventricular system was greatly dilated, and only a thin rim of cortex remained. It was thought that this might be explained on the basis of long-continued interference with

the circulation and venous return. The patient was Rh positive. An examination of the placenta showed the cords to be well knotted and both arose close together near the center of the placenta.

CASE 4.—Mrs. Z. M. (patient of Drs. Walter Levy and Zachary Wohl) was 33 years of age and had one previous baby in 1949, by cesarean section because of contracted pelvis. With this pregnancy the last menstrual period was July 5, 1950, and expected date of delivery April 12, 1951. The pregnancy was uneventful, the labor starting spontaneously April 11, with contractions every five minutes. Because of the previous section, a second low cervical cesarean section was performed, and twins were found. One was macerated and had obviously been dead for some time. The other, who weighed 4 pounds, 4½ ounces, was in poor condition. He was resuscitated and is now in good condition. The amniotic fluid was dark, and the cords of the two babies had to be untangled so that they could be delivered, as the cords were knotted and twisted about the bodies of the babies. A description of the placenta follows: "The placenta is 23 cms. in diameter and two umbilical cords arise near the center. One cord is 36 cms. long and exhibits kinking and atrophy in segments (this was the cord of the macerated infant). The other cord is 25 cms. long and there is no evidence of kinking. The longer one was that of the stillborn baby and was the one principally concerned in the entanglement. There was no evidence of partition or remnants anywhere."

CASE 5.—Mrs. G. M. (patient of Dr. Katherine Havard) was aged 19 years and a primigravida. The last menstrual period was Sept. 1, 1950, and the expected date of delivery was June 8, 1951. The pregnancy was uneventful, and the patient started in premature labor on April 7, 1951. The total labor was two hours, and membranes were ruptured artificially at delivery. The first baby presented by the vertex, and was delivered spontaneously, after a spontaneous rotation from right occipitoposterior to right occipito-anterior position. This baby weighed 5 pounds, 14½ ounces. The second was a face presentation and the baby delivered spontaneously three minutes later. She weighed 3 pounds, 4½ ounces. Both babies received routine premature care and seemed to be thriving. However, the firstborn infant developed abdominal distention and died of peritonitis on the ninth day of life. On autopsy the infection was seen to arise from the appendical area. The second infant developed normally. The placenta showed the typical characteristics, there being no septum or remains of one between the cords or on the fetal side of the membranes. The cords were very short, arose close together and were not knotted or twisted together in any way. Unfortunately, we were not able to obtain a photograph of this specimen.

There is no method by which the presence of this rare condition can be discovered before delivery. It can be diagnosed by the absence of a second bag of waters after delivery of the first twin, or by finding the knotted cords after delivery of the first twin.

The rapid delivery of the second twin where the cords are knotted or tangled is the best way to insure his survival. This should be done by forceps or version and breech extraction.

References

1. Quigley, J. K.: *AM. J. OBST. & GYNEC.* 29: 345, 1935.
2. Béla, G.: *Budapesti orvosi ujság* 35: 318, 1937.
3. Potter, E. L., and Crunden, A. B.: *AM. J. OBST. & GYNEC.* 42: 870, 1941.

DYSTOCIA DUE TO HORSESHOE KIDNEY

A. D. SUMMERS, M.D., PRINCETON, N. J.

(From the Department of Obstetrics, Princeton Hospital)

SEVERAL case reports of dystocia due to ectopic pelvic kidney have appeared in the literature. According to Siegel,¹ who reported a case in 1946, the first published report of this complication occurred in 1880 by Huter.² In 1898 Cragin³ reviewed five previously reported cases and added one of his own. A search of the literature has failed to reveal any cases in which a horseshoe kidney was the cause of dystocia. Because of the unusual character of this case and the favorable outcome for both mother and child, it is worth recording.

A 20-year-old primigravida had been under the care of a physician in a distant city from early pregnancy through the sixth month of gestation. She was referred to me by Dr. R. J. Pierson of Hopewell, N. J. The only significant item in this patient's past history was an attack of appendicitis in April, 1950. The attack was not severe and she recovered without surgery. Her last menstrual period was April 15, 1950, and the estimated date of delivery was Jan. 23, 1951. Her antenatal course was without incident and nothing unusual was noted when pelvic examination was made at her first visit. This patient was of unusually small stature and her nonpregnant weight was 95 pounds. At term she weighed 115 pounds.

The patient went into labor on Jan. 27, 1951. When she was first examined in the labor room the head was at the inlet but not firmly engaged; the fetal heart tones were good and the patient was having strong contractions about every five minutes. On rectal examination the cervix was found to be effaced and 3 cm. dilated. A rounded mass was felt in the upper left quadrant of the pelvis, about 5 cm. by 6 cm., and somewhat the shape of a tangerine. The mass seemed firm, fixed, and did not cause any pain when palpated. An abnormal presentation was suspected, therefore x-rays were done, including pelvimetry. The x-rays did not visualize the mass. The baby's head was dipping into the inlet and the pelvic measurements were said to be adequate.

We now suspected that we were dealing with a pelvic tumor causing dystocia. The patient progressed to full dilatation but there was no advancement of the head. With the patient under inhalation anesthesia, it was possible to dislodge the mass upward over the pelvic brim and then, with fundal pressure, the baby's head engaged and labor progressed normally with spontaneous delivery of a 7 pound, 1 ounce female infant, after a total of 20 hours of labor. Both mother and baby did well and were sent home in good condition on the seventh postpartum day.

When examined, at six weeks post partum, the uterus was well involuted. The rounded mass could still be palpated in the left pelvis and as previously found it seemed to be fixed. I advised the patient to have an exploratory laparotomy done to determine the nature of the mass and to have it removed if necessary. On June 15, 1951, the patient was operated upon by Dr. J. C. Hiden of Princeton Hospital. The uterus was well involuted and in good position; both tubes and ovaries were normal. The mass was retroperitoneal and was thought to be the left kidney. However, on palpation of the region of the right kidney, none was found. There was no kidney in the normal area of the left side. No attempt at correcting the position of the kidney was made. The appendix was removed and the wound closed. Recovery was uneventful.

Before the patient was discharged an intravenous pyelogram was done which revealed a single kidney, lying in the true pelvis, diagnosed as a horseshoe kidney.

In retrospect we believe that the possibility of ectopic kidney should have been considered before surgery was done. However, in reviewing the literature, we find that others who have encountered this condition have made the same error in diagnosis. Waters⁴ referred briefly to a similar case in which the correct diagnosis was made at operation.

I am indebted to Dr. Ralph J. Belford of Princeton and Dr. John D. Preece of Trenton for their advice and assistance in the management of this case.

References

1. Siegel, Irving: AM. J. OBST. & GYNEC. 51: 280, 1946.
2. Huter, E.: Ztschr. f. Geburtsh. u. Gynäk. 5: 17, 1880.
3. Cragin, E. B.: Am. J. Obst. 38: 36, 1898.
4. Waters, E. G.: Bull. Margaret Hague Maternity Hosp. 4: 43, 1951.

71 PALMER SQUARE

SALMONELLA SUIPESTIFER VAR. KUNZENDORF INFECTION IN THE PUERPERIUM*

H. CLOSE HESSELTINE, M.D., AND EDWIN C. TURNER, M.D.,** CHICAGO, ILL.

(From The Department of Obstetrics and Gynecology, The University of Chicago, and
The Chicago Lying-in Hospital)

INFECTIONS with *Salmonella suispestifer*, var. *Kunzendorf* in the parturient woman have rarely been reported in the literature. In the new Chicago Lying-in Hospital, in only one delivery has such an infection been recognized. The literature generally refers to this organism as *S. suispestifer*. This term is synonymous with *S. choleraesuis*, according to Bergey.¹ The organism has the same fermentation reactions as does *S. schottmülleri* except those with arabinose, inositol, and trehalose, which are fermented with the production of acid and gas by *S. schottmülleri*, but are not affected by *S. suispestifer*. There are several varieties of *S. suispestifer*, including the Kunzendorf, or western European variety, and the American variety. The Kunzendorf variety has a greater tendency to invade the blood stream than any of the other animal *Salmonellas*.²

Goulder, Kingsland, and Janeway,³ made a review of the literature concerning *S. suispestifer* infections in 1942. In addition to the literature, they listed eleven cases of such infection occurring in Boston; two of these cases, both being bacteremia and endometritis, were in parturient women. One of the latter two cases was complicated by a sacroiliac arthritis. The other had no complications.

Neter, Siegel, and Clark⁴ in 1944 described an infection of *S. suispestifer* in a gravida at thirty-two weeks' gestation. The patient was febrile, and also was toxic, with hypertension and albuminuria. She went into premature labor ten days after the onset of fever, and delivered a macerated, stillborn fetus. No report was made concerning the presence of the organism in the fetus.

In 1937, Harvey⁵ reviewed the literature quite completely and reported twenty-one new cases of sporadic infections with *S. suispestifer*. He makes no mention of puerperal infections with this organism, but comments that 20 per cent or more of the infections are associated with arthritis or osteomyelitis. He also points out the occurrence of the infection with this organism following surgical procedures.

Case Report.—This 23-year-old para 0, gravida ii, white patient was first seen at six weeks' period of gestation. The one preceding pregnancy terminated by spontaneous abortion. The prenatal course during this pregnancy was normal throughout. After a labor of five hours, thirty-two minutes, she delivered a 2,160 gram, normal living female infant, by the aid of low forceps, on March 11, 1948. The customary left mediolateral episiotomy was performed to facilitate delivery. There were no lacerations of the cervix nor of the vaginal mucosa, and the episiotomy did not extend.

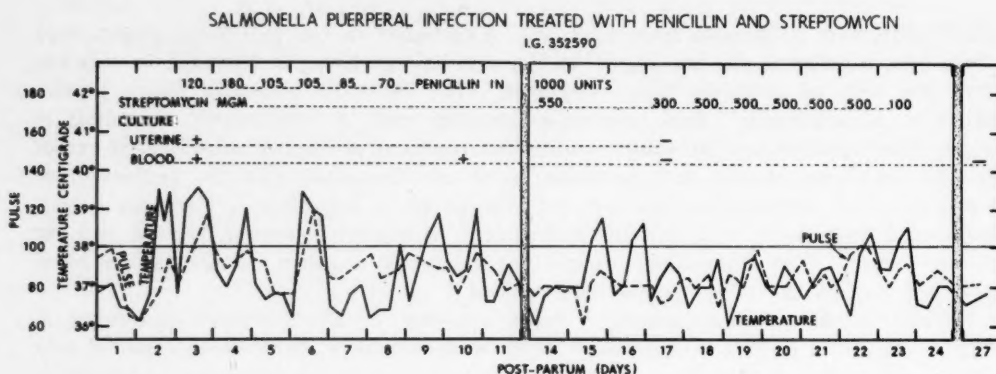
Twenty hours after delivery, the temperature rose to 39.3° C. In spite of the elevated temperature, the patient was free from complaints and the physical and laboratory findings were normal. Blood and intrauterine cultures taken on the following day at the peak temperature of 39.5° were positive, and an organism belonging to the *Salmonella* group was isolated from both sources. Some weeks later it was classified as *Salmonella suispestifer*, var. *Kunzendorf*.† A total of 665,000 units of penicillin was given during the first eight febrile days without altering the course (a full therapeutic amount should not have affected this

*Supported in part by The Chicago Lying-in Hospital Fiftieth Anniversary Research Fund on Puerperal Fever.

**The assistance of Dr. K. Eileen Hite is acknowledged and appreciated.

†This classification was completed through the courtesy of Dr. P. R. Edwards,² Bacteriologist, Department of Animal Pathology, University of Kentucky, Lexington, Ky.

organism). A blood culture taken on the eighth day recovered the same organism. The patient remained afebrile for the next four days. On the fourteenth day post partum, 550 mg. of streptomycin were given, and the next day the patient again became febrile and remained so for nine days. During the last six days of this period of elevated temperature, streptomycin was given to a total of 2,700 mg. Blood cultures taken at the beginning of this period were sterile. At no time did pelvic examination reveal abnormal findings. The temperature fell to normal following discontinuance of the streptomycin, and, after four afebrile days, the patient was discharged. Stool cultures were repeatedly free from these pathogens. The white blood count varied between 5,000 and 10,000. Urine examination occasionally showed a few pus cells (Fig. 1).



On the day after discharge the patient developed severe lumbar pains and the next day had chills and fever. She was readmitted on the thirtieth day post partum, with a temperature of 38.3° C., which rose to 39.6° C. after a chill. She appeared to be in severe pain and was unwilling to move because of pain which was located in the back at the costovertebral angle. The abdomen was tender to palpation, but the pain was always referred to the back. Catheterized urine showed occasional white blood cells and twenty red blood cells per high-power field. Blood cultures were negative. The temperature remained elevated for seven days, during which time intravenous pyelograms showed no abnormality. Repeated uterine and urine cultures now both showed *Streptococcus viridans* and *Bacillus coli communis*. Pelvic examination revealed no abnormal findings. She was then afebrile for six days. Then the temperature rose for four days, during which time an x-ray showed a low-grade infectious lesion at the level of the first lumbar vertebra. The orthopedic service advised a brace for her back. After ten days without fever the patient was discharged on May 8, the fifty-ninth postpartum day.

On May 24 she was seen in the postpartum clinic, at which time she had no complaints nor abnormal findings.

She was seen in Orthopedic Clinic on June 12, complaining of more back pain, weakness, and fatigue. X-ray pictures showed unfavorable progress of the osteomyelitis of the first and second lumbar vertebrae, and suggestive involvement of the right sacroiliac joint. On July 18 she was still having pain, and x-ray pictures showed slight forward slipping of the second lumbar vertebra. A week later the patient was admitted to the orthopedic service at Billings Hospital, where, on July 29, a spinal fusion of the twelfth thoracic to the third lumbar vertebra was performed with a large tibial bone graft. Blood cultures on July 30 and August 2 showed no growth. The postoperative course was uneventful. She was discharged on August 17 in a cast. This cast was removed on the following February 28. She was last seen in Orthopedic Clinic on September 24, at which time she had no complaints referable to the back, but was found to be pregnant. She was referred back to Chicago Lying-in Hospital for prenatal care of this pregnancy. She delivered a normal full-term

female infant weighing 3,295 grams on June 7. Delivery was spontaneous, the postpartum course was uneventful, and there were no evidences of recurrence of the old infection during pregnancy, labor, or the puerperium.

She was asymptomatic and clinically cured two years after the delivery.

Summary

A *Salmonella suipestifer*, var. *Kunzendorf*, infection is reported in the postpartum patient. The infecting organism was recovered from blood and intrauterine cultures. Subsequently, a process localized in the first and second lumbar vertebrae, presumably caused by this organism. This process required orthopedic surgical treatment.

Salmonella suipestifer, var. *Kunzendorf*, infections are relatively rare in the United States, particularly in the puerperal patient. The reports of three cases in the puerperal and prenatal period have been found in the literature. This is a report of the fourth case.

References

1. Bergey, D. H., Breed, R. S., Murray, E. G. D., and Hitchens, A. P.: Bergey's Manual of Determinative Bacteriology, ed. 5, Baltimore, 1939, The Williams & Wilkins Company, p. 440.
2. Edwards, P. R.: Personal communication.
3. Goulder, N. E., Kingsland, M. F., and Janeway, C. A.: New England J. Med. **226**: 127, 1942.
4. Neter, E. R., Siegel, L. A., and Clark, Phyllis: AM. J. OBST. & GYN. **48**: 222, 1944.
5. Harvey, A. M.: Arch. Int. Med. **59**: 118, 1937.

Department of Book Reviews

EDITED BY PHILIP F. WILLIAMS, M.D., PHILADELPHIA, PA.

Review of New Books

Obstetrics

This very well-written text represents a series of four lectures dealing with the **Pathology of Obstetrics**.¹ It is divided into three parts, the first of which deals with the pathology of pregnancy, the second with pathologic delivery, and the third with the pathology of the puerperium. It is interesting to note that the author's treatment of the toxemias of pregnancy, both prophylactic and curative, involves relatively low protein diets and the limitation of fluids.

In dealing with occiput posterior, he favors allowing spontaneous rotation, anteriorly, and if this does not occur and it is found easier to rotate the head posteriorly, this is carried out and the head delivered by forceps. This is in agreement with the attitudes in many clinics in this country.

All in all, the textbook is well written and is an excellent reference for medical students and specialists.

RUSSELL R. DE ALVAREZ

Cunningham's **Textbook of Obstetrics**² resembles other Dublin texts in that it is short, concise, and definitely written for the student in the midst of his practical work on the wards. The methods described are those practiced at The National Maternity Hospital and used in accordance with the ethical standards of the Roman Catholic Church.

There are twelve sections beginning with a description of the female genitals and covering the physiology of pregnancy, normal pregnancy, pathological pregnancy, pathological labor, the puerperium, etc.

Unfortunately, the brevity of this text is not achieved by the deletion of superfluous material but by superficial and occasionally inaccurate treatment. Thus, the sections on the treatment of eclampsia and of heart disease complicating pregnancy leave much to be desired. Cesarean section is recommended for delivery in the latter disease, if there has been a history of decompensation. Acute yellow atrophy is still classed as one of the toxemias and not one mention is made of its possible relationship to infectious hepatitis, and hypoglycemia is given as one of the major causes of neonatal death in diabetic pregnancy. Pain relief in labor is given but a passing nod.

All in all, this book does not come up to the high standards of Irish obstetrics nor can it be considered adequate for the American student.

LOUIS M. HELLMAN

This little volume of 200 pages, **Pratique Obstetricale**,³ by B. Jamain, is intended as a syllabus for the busy practitioner of obstetrics, to aid him in making up his mind as to the proper steps to take when faced with obstetric emergencies and in formulating

¹**Patologia Obstetrica.** By Dr. Jose Botella Llusia, Division of Gynecology of the Faculty of Medicine of Madrid, Spain. 580 pages. Madrid, 1950, Editorial Cientifico Medica. 223 Pesetas.

²**Textbook of Obstetrics.** By John F. Cunningham, Professor of Obstetrics and Gynecology, University College (N.V.L.), Dublin. 499 pages with 297 illustrations. New York, 1951, Grune & Stratton. \$7.50.

³**Pratique Obstetricale.** By B. Jamain, Gynecologue-Accoucheur des Hopitaux de Paris. 200 pages with 8 illustrations. Paris, 1951, L'Expansion Scientifique Francaise.

indications for treatment. The majority of common obstetric conditions encountered by the general practitioner are reviewed briefly but clearly. The only technical procedure to be illustrated in the whole book is the application of forceps by line drawings of the caput. No pretense is made as to completeness of text. The author's aim is to summarize concisely the practical experience gained from the masters of the Baudelocque Clinic. His aim is modest, his purpose worthy; namely, to make known a systematized practice of obstetrics, giving a maximum of safety.

ISIDORE C. RUBIN

Beck's **Obstetrical Practice**,⁴ in the new fifth edition, reflects the extensive research in recent years and the new knowledge of the physiology of the pelvic organs and the changes in them during pregnancy. These additions to our knowledge have necessitated a rewriting of many chapters in the earlier portion of the book. Especially, one may note the sections on implantation and early development of the fertilized ovum, the physiology of the placenta, and the physiology of the fetus.

There is evidence of a very thorough inclusion of the new material on physiology of labor, the complications of pregnancy, and inertia uteri. Beck has added another beautifully illustrated mechanism of labor, that of L.O.T., transverse position of the head.

This book must be regarded as one of the outstanding single-volume texts on the practice of obstetrics.

PHILIP F. WILLIAMS

Maternity Care in Two Counties⁵ is a report of a study of the maternity care services in Gibson County, Tenn., and Pike County, Miss. Data for the study were obtained from all available records in the two County Health Departments pertaining to maternity cases terminating in the years 1940, 1941, 1943, and 1944, and from review of cases with physicians.

Quoted from Introduction, page ix: "The extent to which antepartum services, both medical and nursing, were utilized by various groups of the population is recounted; complications of pregnancy are discussed, with the discussion based on data about all maternity patients who were under the supervision of health department nurses during the antepartum period; the delivery service cases are reviewed, first from the standpoint of management of labor and delivery, and, second, from that of administrative details of a delivery service; postpartum care, both medical and nursing, is described; and maternal mortality and mortality of offspring are analyzed."

There are fifty-six tables in the text and seventeen additional tables in an appendix. There is an adequate index. The report gives ample evidence of the need for more and better medical, nursing, and hospital service, to say nothing of education for those women who bear and rear our children on the back roads of America where the surface of the socioeconomic problem has not yet been scratched.

HAZEL CORBIN, R.N.

The current edition of the **Year Book of Obstetrics and Gynecology**⁶ covers, in abstract, articles which appeared between August of 1950 and June of 1951.

This edition presents, as have all similar editions in the past, the eternal dichotomy between the passing and the permanent. In the articles themselves one does not expect

⁴**Obstetrical Practice.** By Alfred C. Beck, M.D., Professor Emeritus of Obstetrics and Gynecology, State University of New York, College of Medicine at New York City. Fifth edition. 1073 pages with 947 illustrations. Baltimore, 1951, The Williams and Wilkins Company.

⁵**Maternity Care in Two Counties.** By Frank E. Whitacre, M.D., Chief, Division of Gynecology and Obstetrics, The University of Tennessee College of Medicine, and Ellen Whiteman Jones, M.P.H., Statistician, The Commonwealth Fund. 165 pages with 56 tables. New York, 1950, The Commonwealth Fund. 50 cents.

⁶**Year Book of Obstetrics and Gynecology—1951.** Edited by J. P. Greenhill, B.S., M.D., F.A.C.S., Professor of Gynecology, Cook County Graduate School of Medicine. 567 pages with 130 illustrations. Chicago, 1951, The Year Book Publishers.

to find the distilled and permanent truths of the speciality; the very fact that a new edition is justified each year would indicate that this is not the function of these books. These abstracts serve a more modest (but nevertheless useful) function in reflecting accurately the current gynecologic beliefs and standards as preached by thoughtful practitioners. They are current; they are contemporary; they are also temporal, and one needs only peruse the Year Books of a decade ago to realize how passing so many of them are.

On the other hand, the editor's comments provide a permanence and stability to these volumes. As the clinical suggestions rise and fall, as the fads come and go, the opportunity for the editor to comment is also the opportunity to spin the strand of consistency and continuity.

Thus, for example, reviewing the topic of the Induction of Labor. Over the past decade, successive Year Books have carried abstracts advocating Pituitrin, ergot, Pitocin, quinine, castor oil, the rectal tube, and so on. The editorial comments, on the other hand, have reflected Dr. Greenhill's consistent advocacy of stripping and rupturing the membranes, and his firm insistence on the ripe cervix as a prerequisite. Or, again, considering the topic of the use of the estrogens in labor: in 1937 the estrogens were suggested to induce labor (the editor had not used them); in 1940 they were again urged for the induction of labor (no editorial comment); in 1943 it was recorded that the estrogens increased the motility of the laboring uterus (the editor mentioned the work which indicated that the estrogens quieted uterine activity); by 1945 the editor found himself in agreement with the then relatively new theory as to the role of the estrogens in threatened abortion, a position he has continued to maintain.

There is a sameness here which is also fortunately a saneness. Dr. Greenhill's comments reflect a perception and a conservatism which are commendable. The current edition of the Year Book again reveals well the passing scene and one man's opinions of that scene.

ALLAN C. BARNES

Gynecology

In the book, **Psychosomatic Gynecology**,⁷ the authors attempt to present the psychodynamics of certain problems occurring in gynecology and obstetrics. They state that their purpose is to provide a workable knowledge of the psychodynamics of disease for the physicians specializing in obstetrics and gynecology. Briefly, the psychodynamic patterns, as presented in the book, are fundamentally those of Freud. The first portion of the book deals with the psychosomatic aspects of the fetus and infant. In this section the effects of the prenatal care, as well as the care of the mother during labor and delivery and during the puerperal period, are considered from the viewpoint of the ultimate effect on the child. This is followed by discussion of psychosexual development of the infant in which the original Freudian theories are outlined.

The second part deals with the psychosomatic aspects of the mother during pregnancy and hinges largely upon the work of Grantly Dick Read and the use of hypnosis during labor. It covers, in addition, nausea and vomiting, ptialism, abnormal appetite, lactation, pseudocyesis, dysmenorrhea, and premenstrual tension.

In part four, some of the more common gynecological psychosomatic problems are discussed, including contraception, sterility, frigidity, dyspareunia, low back pain, pelvic pain, menopause, pruritus, and the congestion fibrosis syndrome. The book concludes with a section on methods of diagnosis and treatment.

One of the best features of the book is the excellent and well-placed bibliography which makes it possible to check the references readily. Unfortunately, the book falls far short of its original aim. The average practitioner of obstetrics and gynecology certainly will not be sympathetic with the psychodynamic explanations given. For instance, there is a chapter devoted to pre-eclampsia and eclampsia in which it is suggested that

⁷**Psychosomatic Gynecology: Including Problems of Obstetrical Care.** By William S. Kroger, Assistant Clinical Professor of Obstetrics and Gynecology, Chicago Medical School and S. Charles Freed, M.D., Adjunct in Medicine, Mount Zion Hospital, San Francisco, Calif. 487 pages. Philadelphia and London, 1951, W. B. Saunders Company. \$8.00.

the etiology may well be psychosomatic. There is a similar chapter entitled "Emotional Spontaneous Abortion." The extreme is reached in the discussion on cystocele, stress incontinence, and fibroids, in which it is suggested that these, too, may be of psychic origin. Single case histories are used as proof of the author's contentions, a technique which makes reading enjoyable but unscientific. The cases are invariably of a bizarre nature.

Strangely enough, there is no discussion of postpartum depression, which is a fairly common disorder. Similarly, the influence of organic disease on the patient's psyche is not given its due importance. A recent editorial in the *New England Journal of Medicine*, Nov. 15, 1951, entitled "Stark Unreality," hits the nail pretty well on the head when it states, "The movement is far enough out of critical hands to permit the gullible, unknowing public to believe that it can worry itself into heart disease, hypertension, and thyrotoxicosis—in addition to peptic ulcer—or, shortly, if divinations go on apace, into almost any disease that has previously been classified as predominantly of organic or exogenous origin. Although popular and semi-scientific journalism are inculpated, the too enthusiastic and uncritical psychosomaticists themselves are primarily responsible."

The authors freely admit that much of the material in the book will be controversial. It would seem better to use the words "highly speculative."

JAMES F. DONNELLY

This practical volume, **Malignant Disease of the Female Genital Tract**,⁸ is based on the extensive experience of the author, who is gynecologist to the Newcastle Regional Cancer Organization. An excellent feature of the book is the inclusion under one cover of contributions of subject matter often separately published in organs of the radiotherapist and the pathologist. The orderly, pedagogical arrangement of the subject matter leads to ready availability of sought-for information. Numerous tables condense facts which otherwise would require many pages for elucidation. While the general treatment is concise, extensive bibliographies are appended to the several chapters. It is regretted that colored illustrations of lesions did not find their way into this volume. The reviewer also believes that not sufficient emphasis and recognition are given to the value of screening techniques, using surface biopsies and stained spreads from the cervix. Abbreviated also is the author's account of interesting biologically active ovarian tumors. The significance of the manner of spread through the lymphatics of the various malignant lesions is repeatedly indicated, and the author rightly admonishes against reliance on single negative biopsies of suspected lesions which may be quite meaningless.

The text is well written and covers the more common malignant gynecological lesions; the relative merits of the various therapeutic methods are plainly discussed, and the importance of early diagnosis emphasized. Busy practitioners and students should find this working volume a valuable addition to their libraries.

W. T. POMMERENKE

This 68-page, paper-backed booklet, **Zur Klinik des Korpuserkarzinoms**,⁹ is published as a supplement to volume 135 of the *Zeitschrift für Geburtshilfe und Gynäkologie*. It is dedicated to Walter Stoeckel in honor of his eightieth birthday.

The material encompasses 303 cases of cancer of the corpus uteri encountered in the Kiel Clinic between the years 1922 and 1945. The text is in German and in places suffers, for this reviewer, from sentences of paragraph length. This however does not lessen the basic value of Dr. Huber's critical and excellent presentation.

It is interesting to note that 20 per cent of the patients in this study were under 50 years of age, while the youngest was 26. She is still well 25 years after operation.

⁸**Malignant Disease of the Female Genital Tract.** By Stanley Way, Gynecologist to the Newcastle Regional Cancer Organization Association. 279 pages with 38 illustrations. Philadelphia, 1951, The Blakiston Company. \$5.00.

⁹**Zur Klinik des Korpuserkarzinoms.** By Prof. Dr. Herbert Huber, Oberarzt der Univ. Frauenklinik, 68 pages with 25 illustrations. Stuttgart, 1951, Ferdinand Enke. 12 marks.

The pathology of corpus cancer is well discussed, not in minute detail, but sufficiently well to give the clinician what he requires. At the same time it is evident that the author understands this basic phase of his subject. This is reflected in a refreshing and wholesomely sound approach to his problem.

Part two of this booklet is given over to an excellent discussion of the methods of treatment for corpus cancer and it is the author's conclusion that surgery offers the best outlook for cure in this disease. Dr. Huber's discussion of the problem of the clinical determination of operability versus inoperability is realistic and thorough.

Part three is devoted to a grouping of his material on the basis of demonstrable anatomical findings. The varying incidence of curability is then determined and correlated to verifiable gross and histological studies.

Throughout this study the author expresses himself as being impressed by the tendency for occurrence of other multiple primary pelvic generative tract tumors in association with corpus cancer. He considers this more than coincidental and probably due to a uniform localized systemic tumor stimulus confined to an organ such as the uterus or closely related organs, such as the tubes and ovaries.

The booklet is unreservedly recommended.

KARL H. MARTZLOFF

The experience and ability of the author of *Gynecologic Cancer*,¹⁰ as a worker and teacher in the field of pelvic cancer, are evidenced throughout the entire text. In the introduction, thorough consideration is given to the problem of early diagnosis and the responsibility for delay. After emphasizing the need for early diagnosis and carefully reviewing the methods available, the author begins at the vulva and considers in each succeeding chapter the site involved as one advances up the birth canal and into the pelvis. Surgical and radiological methods are described for each type of the disease. For the most part the references to the surgical treatment are scant and far less complete than the discussion of irradiation therapy, which the author understands and describes so well. Although this reviewer agrees entirely with the thought that irradiation therapy is the method of choice in most gynecologic cancer, those seeking information relative to the more radical surgical procedures in vogue today would have to turn to such reports. The text is of value to all physicians dealing with pelvic malignancy and is a must for the young trainee.

HERBERT E. SCHMITZ

The monograph, *Über die Röntgenologischen Darstellungsmöglichkeiten des weiblichen Genitalapparates mit Hilfe von Jodol und Jodsol*,¹¹ by J. Erbslöh consists of three parts: (1) The physicochemical basis of contrast media commonly employed in gynecology, (2) conclusions and results, and (3) clinical investigations. The first and largest part is taken up with theoretical discussions of the physicochemical aspects of the contrast media, much of which concerns viscosity, surface tension, and their wetting property. The clinical gynecologist will not be interested in viscosimeters or in mathematical equations and chemical formulary of the substances considered. But, for x-ray specialists and certain gynecologists with special curiosity, there is a good deal of rewarding interest in these basic aspects.

The second part discusses the desiderata of an ideal contrast medium and presents advantages and disadvantages of oily and water-soluble iodine substances. Erbslöh has preferred the latter because of lesser viscosity and better wetting property essential for hysterosalpingography. The agent he uses is called Hepatoselactan or Vasoselectan, originally devised by Degkwitz and made by Schering A. G. It has the advantage of better

¹⁰*Gynecologic Cancer*. By James A. Corscaden, M.D., Professor Emeritus of Clinical Gynecology, Columbia University, and Attending Gynecologist, Sloane Hospital for Women, New York City. 361 pages with 110 figures. New York City, 1951, Thomas Nelson & Company. \$6.00.

¹¹*Über die Röntgenologischen Darstellungsmöglichkeiten des weiblichen Genitalapparates mit Hilfe von Jodol und Jodsol*. By Doz. Dr. Med. Habil. J. Erbslöh, Bad Oldesloe. 74 pages with 64 illustrations. Stuttgart, 1951, Georg Thieme. D. M. 16.80.

diffusion after intra-amniotic injection than that obtained with the use of oily iodine preparations and, according to the author, it also demonstrates better contrasts of tubal and cervical mucosa, giving relief pictures of the tubal plicae. Responsible for this physical property is the change brought about by converting iodized oils into colloid solutions. Jodsol (Hepatoslectan) has been produced in this way. It is said to be superior to other water-soluble iodine solutions by obviating the hypertonicity of the latter which ordinarily provokes abdominal pain. Jodsol is isotonic and thus causes no more irritation than the iodized oils. Originally devised for intra-amniotic injection to localize the placenta, Jodsol has not proved satisfactory for this purpose and Erbslöh has adopted it for use in gynecology.

This work is a serious attempt to elucidate some of the basic principles of contrast media commonly employed in hysterosalpingography. While not exhaustive by any means, a number of moot points still remaining to be solved, it is nevertheless well worth reading and studying by the practical gynecologist, as well as the roentgenologist who employs x-ray contrast media for diagnosis.

ISIDORE C. RUBIN

This volume, **Symposium on Steroids in Experimental and Clinical Practice**,¹² is a collection of presentations concerned with the biological effects of lesser known synthetic steroids, and the discussion of them by qualified American investigators. The conference was held earlier this year in Mexico and the hope is expressed that similar meetings will occur annually hereafter. Syntex, S.A., the amazing young Mexican chemical concern that derives its steroids from a copious, inexpensive, inedible native yam, sponsored the conference. In the process of producing steroids of known usefulness, large quantities of steroid intermediates and by-products become available. Investigators have been feverishly attempting to evaluate these compounds in the laboratory and clinically in the hope of finding cheap plentiful substitutes for cortisone and related biologically active steroids. One of the most abundantly available intermediates is Δ^5 pregnenolone and the major portion of the conference dealt with it. Unfortunately, the clinical reports regarding the activity of the uncommon synthetic steroids and Δ^5 pregnenolone, in particular, have been conflicting. Primarily the conference was designed to resolve if possible the discrepant results observed notably in the arthritides.

Twenty-three papers were presented, one of which is a lengthy discerning commentary by Dr. A. White who served as editor of the volume. His remarks were devoted to the evaluation of six preceding papers that were concerned with nonclinical investigative work. The remainder of the reports deal with clinical observations. Of particular interest to members of our specialty would be the singularly favorable results reported using Δ^5 pregnenolone for seminal inadequacy in infertile men. Also, there is an interesting report on the use of progesterone in cervical carcinoma. The photographs accompanying the latter show a most impressive surface healing of the lesions.

There is an excellent section devoted to the use of steroid hormones in neoplastic diseases generally and mammary carcinoma in particular. The clinical reports are well documented and include considerable biochemical metabolic data derived from patients under therapy. One of the most valuable features of the volume is the recorded discussions by the participants in the conference. From these discussions the reader achieves a vantage point from which to appreciate the intrinsic difficulties encountered in the clinical evaluation of a steroid compound. Further and perhaps more important, the reader can derive a critical interpretation of the presented data from prominent hormonologists and rheumatologists. Finally, at the end of the volume, there is a rather comprehensive tabular summary of all the clinical results reported at the meeting. Unfortunately, the information that can be obtained from the tables is too pat for this reviewer's taste. At best it represents a skeleton of the body knowledge. The muscle and sinew

¹²**Symposium on Steroids in Experimental and Clinical Practice.** By Abraham White, M.D., University of California Medical Center, Los Angeles, Calif. 415 pages with 103 figures and 104 tables. Philadelphia, 1951, The Blakiston Company. \$7.50.

of the conference are to be found in the papers themselves and particularly in the opinions expressed during the discussion of the reports.

This book should be of interest in a general way to anyone undertaking the clinical evaluation of a steroid compound because there is repeated emphasis on the many variables that must be explored or controlled to constitute an adequate study. To those primarily interested in a most comprehensive picture to date of the biological behavior of Δ^5 pregnenolone this book is recommended.

RALPH B. WOOLF

Going out from historical considerations, the author, in his book, **Mammoplastik**,¹³ elaborates on the modern concepts of the ideal shape of the female breasts. He then stresses the various indications for breast plasty and the proper selection of the patient. The various penduloses are divided into simple, atrophic, and hypertrophic forms. The author prefers for correction of pendulous breasts only those operations which preserve the function of the gland. In the majority of patients a one-stage procedure is possible. In extreme cases, however, he considers the two-stage procedure safer. For the one-stage procedure he chooses a method similar to the Lexer type operation, and for the two-stage procedure the areolar flap method after H. May. The author describes only those methods with which he has personal experience, hence the scope of the book is quite limited. The drawings as well as the results depicted in pre- and postoperative photographs are good. The book can be recommended to those who are interested in the subject.

HANS MAY

In preparing the third edition of their work, **The Diagnosis and Treatment of Menstrual Disorders and Sterility**,¹⁴ Drs. Mazer and Israel have revised extensively. Much new material has been added which modernizes and brings up to date this interesting book.

As one has come to expect from previous editions, the authors are not too sharply bound down by their title. The book includes a discussion of carcinoma of the cervix, outlines the techniques for cervical biopsy, presents a clinical evaluation of the Papanicolaou smear, and ranges through such diverse topics as endometriosis, cervical polyps, and artificial insemination.

Predominantly, however, the book continues to reflect the authors' own interest in endocrine therapy. Their strong preference for the "natural" as against the synthetic estrogens is quite apparent, and this edition, like its predecessors, contains the summarized enthusiastic defense of low dosage x-ray over the ovaries and pituitary in the treatment of a variety of gynecologic disorders.

The book also contains an Appendix on Commercially Available Standardized Endocrine Products, which summarizes the appropriate trade names and market form of the various endocrine principles mentioned in the text. Knowing the ebb and flow of commercial nomenclature, and the "new" forms introduced each year, one would feel safe in predicting that this section may well be outdated while the book is still being fondly read by its enthusiasts.

ALLAN C. BARNES

This book, **Renal Pelvis and Ureter**,¹⁵ beautifully composed from the publishing point of view, is a monographic account of a stupendous amount of detailed observation. It suffers, however, from the inability of the author to condense his material. He seems

¹³**Mammoplastik.** By Fritz Schorcher, Professor of Surgery, University of Munich, Germany. 78 pages with 53 illustrations. Munich, Rieger'schen Universitätsbuchhandlung. 1951.

¹⁴**Diagnosis and Treatment of Menstrual Disorders and Sterility.** By Charles Mazer, M.D., Attending Gynecologist, St. Agnes Hospital, Philadelphia, and S. Leon Israel, M.D., Assistant Professor of Gynecology and Obstetrics, Graduate School of Medicine, University of Pennsylvania. Third Edition. 583 pages with 137 illustrations. New York, 1951. Paul B. Hoeber, Inc. \$10.00

¹⁵**Renal Pelvis and Ureter.** By Peter A. Narath, M.D., F.I.C.S., Adjunct Professor of Urology, New York Polyclinic Medical School and Hospital. 439 pages with 264 illustrations. New York, 1951, Grune & Stratton. \$12.50.

to be laboring under the impression that he is presenting many new and revolutionary concepts, and that his best chance of convincing his readers of the truth of these concepts is by seemingly endless repetition of illustrative examples. Some of these concepts are highly theoretical and, as repeatedly admitted by the author, not altogether substantiated by the evidence presented.

As an example of unnecessary repetition, seventy-eight pages with sixty-six illustrations are used to emphasize the tremendous variations in form and configuration that may be encountered in normal pelves and calyces. This is a fact well recognized by everyone with any experience in the viewing and interpretation of pyelograms.

In the opinion of this reviewer by far the best sections of the book are those dealing with resorption and absorption from the upper urinary tracts and with various forms of extravasation. Here certain concepts and interpretations are presented which might well replace the older established habit of grouping most of these phenomena under the single heading of pyelovenous back flow.

The book is one which should be of interest and value to anatomists, physiologists, and ultrascentific urologists, but which may have little appeal to the average reader of this JOURNAL whose primary interest lies in the fields of gynecology and obstetrics.

HOUSTON S. EVERETT

This book, **Atlas of Genito-Urinary Surgery**,¹⁶ is truly an atlas with explanatory notes kept to a minimum. It should fulfill adequately the avowed purpose of the author as stated in the preface, namely, to present standard operative procedures, "in simple form, for the resident who is just coming into contact with urologic surgery, for the practicing urologist who may have need to retrace the steps of an operative technic infrequently performed, and also for the general surgeon who may at times be confronted with the necessity of operation for a urologic problem with which he is not entirely familiar."

The line drawings by Charles Stern are excellent, but in some instances make difficult procedures seem too simple. There is some material in the book which should be of interest to the gynecologist regardless of whether he has an interest in or practices female urology. This is true of the various methods of correcting urethral injury, the operations for vesicovaginal fistula, for stress incontinence of urine, and for suburethral cyst. The techniques illustrated for these conditions are not always the ones that the reviewer would choose, but are good standard ones and therefore a matter of individual choice. The procedure illustrated for urethral caruncle is more extensive than is usually required and is really the circumcision technique described by Kelly for urethral prolapse.

As adequate as this book is in fulfilling its purpose, no atlas or book of any type can ever replace the residency system under competent preceptors in the training of a surgeon. I sincerely hope that it may never be my misfortune as a patient to "be confronted with the necessity of operation for a urologic problem with which he is not entirely familiar" by a general surgeon no matter how competent in his own field and no matter how many atlases he may have available.

HOUSTON S. EVERETT

If one takes the trouble to assess the manner in which surgical thought has progressed in recent years, one cannot help but be impressed with the fact that by and large the emphasis seems to have been along purely technical lines. All too often, attention is focused merely upon the particular surgical lesion and the implications of how the rest of the human mechanism might be affected are either partially or totally obscured. This text, **Surgical Care**,¹⁷ by the author of many contributions on parenteral fluid therapy, presents the broad subject of surgical care from the physiologic aspect.

¹⁶**Atlas of Genito-Urinary Surgery.** By Philip R. Roen, M.D., F.A.C.S., Instructor in Urology, New York Post-Graduate Medical School; Clinical Instructor in Urology, New York Medical College. 325 pages, with 417 illustrations. New York, 1951, Appleton-Century-Crofts, Inc.

¹⁷**Surgical Care, A Practical Physiologic Guide.** By Robert Elman, M.D., F.A.C.S., Professor of Clinical Surgery, Washington University School of Medicine. 586 pages with 182 figures. New York, 1951, Appleton-Century-Crofts, Inc.

Among the chapters dealing with this subject are those on systemic reaction to trauma, psychogenic factors, nutrition, physical factors, basic preoperative care, anesthesia, chemotherapy, postoperative pain, postoperative renal dysfunction, thromboembolic disease, wound and abdominal complications. Admittedly, it would seem somewhat difficult, if not impossible, to cover the entire subject in a reasonably sized text, yet the author and an impressive list of collaborators have done an admirable job.

Especially valuable are the chapters on systemic reaction to trauma, anesthesia, and nutrition in surgery. In the first of these the author presents a very lucid exposition of adrenocortical activity and metabolic changes following trauma; in the second, Dr. Meyer Saklad presents the most rational approach to present-day problems in anesthesia we have seen anywhere, and, in the third, the author has succeeded in putting together the very many useful facts which he and others have learned about this subject in their many studies, especially along lines of parenteral fluid therapy.

All in all, this is a valuable text for all physicians whose practice in any form brings them in contact with the surgical patient.

SEYMOUR SCHOTZ

This book, **Physiotherapy in Obstetrics and Gynecology**,¹⁸ by the author of the popular *A Way to Normal Childbirth* will be welcomed as a more comprehensive exposition of Mrs. Heardman's ideas in adapting physiotherapy techniques to clinical obstetrics and gynecology. An important section is devoted to prenatal breast preparation for lactation. Another section of major interest is devoted to physiotherapy in gynecology. The chapter on anesthesia and analgesia, written by Shila G. Ransom, expresses sound principles which will be heartily endorsed by physicians and nurses in this country who are endeavoring to correct many false impressions about natural childbirth techniques. The final paragraph is a simple but highly eloquent statement: "Analgesic and allied drugs should not, normally, be forced upon a woman who genuinely prefers to do without, but she should know that they are available for her the moment she needs them. Finally, we must always remember drugs can support right management but can never supplant it."

Although the book is written for those whose interests are in the field of physiotherapy, it cannot fail to have appeal to all who are interested in obstetrics and gynecology. In England it is apparent that, following the lead of the author, physiotherapists are becoming part of the obstetric team. Mrs. Heardman recognized, however, that the future alone would decide the manner of development.

This reviewer welcomes this opportunity to pay tribute to Helen Heardman as a pioneer in education for childbirth, whose vision for the future of obstetrics was based upon sound physical and psychologic principles. Her contribution to American obstetrics made through a personal visit to this country some months before her untimely death has already resulted in changes in our obstetric thinking. Fortunately she lived long enough to be aware of these attitudes both here and in her own country. Her book is recommended without reservation to the medical profession.

HERBERT THOMS

Probably no phase of postnatal care is as much neglected as the subject matter of this small but thoroughly illustrated brochure, **Exercises After Childbirth**.¹⁹

The aims of the exercises described will undoubtedly be achieved by faithful adherence. Certainly, the reduction of an unnecessary weight gain during pregnancy and the correction of posture should follow their use.

The contribution is a valuable one to the physiotherapeutic measures now commonly prescribed in certain gynecological and obstetrical conditions.

¹⁸**Physiotherapy in Obstetrics and Gynecology.** By Helen Heardman, M.C.S.P. 228 pages with 91 illustrations. Edinburgh, 1951, E. and S. Livingstone, Ltd. \$3.50.

¹⁹**Exercises After Childbirth.** By Gertrude Behn, M.C.P.S., former Superintendent Physiotherapist, Newcastle General Hospital. 32 pages with 36 illustrations. Edinburgh, 1951, E. & S. Livingstone, Ltd. 50 cents.

The cost of the pamphlet is sufficiently inexpensive that it might be added to the literature which the physician distributes to his patients.

PHILIP F. WILLIAMS

The popularity of **Planned Parenthood**²⁰ is shown by the previous edition having gone through ten printings. This second edition attempts to bring the subject up to date. Of the chapters on social and legal aspects one can only find praise. The discussion of sex anatomy and physiology is adequate for the layman. When we reach the chapters on contraceptive methods, the reader has the distinct impression that the author is thoroughly sold on the diaphragm and jelly method and evaluates other methods at a lower rate of effectiveness than has been found in rather extensive reports from several clinics. He states that the diaphragm has been reported as successful in 95 per cent of cases in a series from New York and Newark Centers. Neither in this discussion nor in the discussions of the pessary does he refer to the report of Eastman and Seibels (J. A. M. A., January 1, 1949), in which Stix and co-workers are quoted as showing from five areas with 108,461 women months of exposure, an average reduction in fertility of 80 per cent (with a high of 88 per cent and a low of 67 per cent) with the use of the diaphragm and jelly method. These authors report on the use of the suppository alone in Baltimore with 4,210 women months an efficacy of 88.9 per cent, when method failure alone is considered, and 88.8 per cent when all failures are figured. In the South Carolina studies (loc. cit.), with 1,573 patients, 21,088 women months, an average efficacy of 94.9 per cent, with a low of 80 per cent and a high of 99.6 per cent. In both the Baltimore and the South Carolina studies no diaphragms were used. In the South Carolina studies, several creams, jellies, suppositories, and sponge and powder were tested. This certainly would suggest that the simpler methods were more efficient than the cumbersome diaphragm and jelly. Following these studies the diaphragm and jelly method was removed from the methods prescribed at Johns Hopkins and in the Public Health Clinics of South Carolina. The author defines the ideal contraceptive as requiring acceptability as one of its essentials. To be acceptable, "the method should be simple in application and care, readily available, convenient, inexpensive and esthetically pleasant," yet we find that it requires 12 pages in his text to describe the fitting, the use, removal, care, learning the use, and testing of the diaphragm and its refitting after childbirth. In describing the use of suppositories, 6 lines are all that are necessary to cover the subject in his text. It seems amazing that the douche should be mentioned as a contraceptive other than to condemn it. If he insists that a mechanical barrier, such as the diaphragm, is necessary, and condemns the suppositories for the lack of a barrier, how can he consider the douche of any value when there is no mechanical barrier effect. Nor does he, we hope, wish us to believe that any type of douche with any type of material will remove sperm which have entered the cervix through direct insemination. Prevention of direct insemination is the only scientific excuse for the diaphragm.

ROBERT E. SEIBELS

The chapters of this authoritative book, **Handbook of Nutrition**,²¹ appeared recently in an abbreviated form as separate articles in the *Journal of the American Medical Association*. Thirty-three noted investigators in the field of nutrition have adequately covered the subject. The metabolism of the individual nutrients, the nutritional needs in health and disease, the pathogenesis of the deficiencies, and a discussion of foods are all well documented.

It is unfortunate that several criticisms can be made about what should be a very useful book. Little of important recent developments is discussed. Thus, in the chapter on nutritional requirements during pregnancy and lactation by Stuart and Burke, the

²⁰**Planned Parenthood.** By Abraham Stone, M.D., and Norman E. Himes, Ph.D. Second edition. 221 pages with 26 illustrations. New York, 1951, Viking Press. \$3.75.

²¹**Handbook of Nutrition.** Symposium prepared under the auspices of the Council on Foods and Nutrition of the American Medical Association. Second edition. 717 pages with 7 charts, 28 tables and 35 figures. Philadelphia, 1951, The Blakiston Company. \$4.50.

latest reference is from 1947. Elsewhere, reference to vitamin B₁₂ is inadequate and dates from 1948. The use of pyridoxine in the nausea of pregnancy is discussed in two sentences with references from 1944; no mention is made of more recent work which casts doubt on its value. The book is printed on paper of poor quality.

Several chapters are outstanding, particularly on fluid therapy by Darrow, vitamins by Youmans, and undernutrition by Keys.

A chapter on American diets could be read profitably by all physicians. On the whole the book can be recommended as a valuable source of clinical nutritional information.

S. O. WAIFE

The important position held by the visiting nurse in community health problems is emphasized in this second edition of **The Public Health Nurse and Her Patient**.²² The subject of the public health nurse and her maternity patient is exceptionally well handled and points out the ways in which the public health nurse may help a pregnant woman's physician in rural areas or crowded city sections.

The discussion of the emotional reactions related to the pregnancy itself and the help the nurse may give the patient could well be studied by the average man with a large maternity practice.

The book is recommended to those who rely on the public health nurse for assistance in the various problems in the practice of medicine.

PHILIP F. WILLIAMS

Let's Have Healthy Children²³ is presented primarily for mothers of infants and young children. It is written by a trained and experienced nutritionist who is devoted to the principle of having healthy children through good natural foods and good psychology. It is a fortunate child whose mother knows the information provided here and will use it. It leaves little for the pediatrician to add about foods.

The diet during pregnancy is extensively considered because of its importance. Entirely adequate ingestion of protein, iron, copper, iodine and other minerals, and vitamins A, B, C, D, E, and K is advised. Sources are presented. Multivitamin capsules are not recommended unless B rich foods are used at the same time. A daily schedule is shown.

The success of nursing is largely determined by adequacy of the diet. Calcium, protein, and the B vitamins are called for. Since dry brewers' yeast is 46 per cent protein or more, contains all the known B vitamins, and is customarily taken in liquid, it becomes the modern substitute for old-fashioned beer.

All babies need supplementary vitamins A, B, C, D, and E, as well as wheat germ oil. Fat-soluble oils are best absorbed when given after meals. Vitamin K is needed for low prothrombin. Iron, copper, and iodine can be easily provided when needed. Supplements are more important for babies born prematurely.

Raw unpasteurized, undiluted, unsweetened certified milk is given first choice for the baby. Evaporated milk has second choice. Undiluted milk plus added yeast are advised for premature babies.

The psychology of the procedure of feeding the baby in regard to time intervals, holding him, rocking, etc., for good feeding habits is presented.

Many of the health problems of infants and children are considered from the experience of the nutritionist. They include vomiting, constipation, the use of enemas, bad-colored stools, diarrhea, teething, diaper rashes, nonallergic eczemas, respiratory tract infections. Frequent feedings are helpful during illnesses. The use of drugs should be left to the pediatrician.

The author writes from experience and conviction. Her style is forceful and interesting. There is not a dull page for one who is interested in the development of

²²**The Public Health Nurse and Her Patient.** By Ruth Gilbert, R.N., Assistant Professor of Nursing Education, Teachers College, Columbia University. Second edition. 348 pages. Cambridge, Mass., 1951, Harvard University Press. \$3.75.

²³**Let's Have Healthy Children.** By Adelle Davis. 314 pages with four photographs. New York, 1951, Harcourt, Brace and Company. \$3.00.

healthy children and particularly for one who has faced the many problems discussed. Adelle Davis recognizes the difficulties today of promoting health in children through optimum food and psychology.

JULIAN M. LYON

Caring for the Premature Baby²⁴ is a worth-while book for the purposes for which it is intended. These purposes are clearly stated in the preface and the author is consistent in accomplishing her objectives. It is written by a registered nurse of experience in care of premature babies who often do not have the advantages of the highly specialized hospital premature nursery. It is especially for mothers, practical and student nurses, midwives, and relatives who need to understand the problems of prematurity as the baby is going through his early days and weeks.

When babies arrive prematurely at home, the safety of the baby has to be guarded by understanding care at birth and in the minutes, hours, and days that follow. The care of the baby and the improvising of equipment are well directed. The attendants are taught the frailties and special needs of the baby in the home for his survival.

Feeding the premature baby under his difficulties is well recognized. The means of administering the food by dropper, gavage, and bottle are detailed.

The premature baby's special needs for A, D, C, and B vitamins and calcium, phosphorus, iron, and sodium intake, due to his loss of the late normal intrauterine development and his subsequent rapid growth, are noted. Available vitamin preparations are discussed. Some disturbances incident to the progress of the premature baby are anticipated. The nurse's handling of such troubles as cyanosis, skin and respiratory tract infections, and thrush are recorded.

The attitude of the author is one of humility in face of the great difficulties in helping the delicate premature baby. The need and desire for medical direction at all times are indicated by the author.

JULIAN M. LYON

This atlas, **Atlas der Pathologischen Anatomie**,²⁵ represents a collection of the typical gross pathologic changes found at the necropsy of human bodies. These changes are illustrated by 564, mostly four-colored, reproductions of photographs of the fresh specimens. The expertly selected material and the masterly reproduced pictures of pathological changes give a true-to-life impression of the fresh specimens. These, with a brief explanatory text, offer very valuable aid to those studying gross pathological changes of the human body, particularly when a great deal of fresh autopsy material is not available.

JOSEPH STASNEY

This text represents the proceedings of the **First Obstetric and Gynecologic Congress in Mexico**.²⁶ The presentations cover ten major fields in obstetrics and gynecology, with a special reference to the mechanism of menstruation, thyrogenital interrelationships, genital tract neoplasms, abortion, genital tract infections, amnesia, analgesia, and anesthesia, the use of forceps, fetal anoxia, and postpartum hemorrhage. Each of these subjects is exhaustively considered, with a review of the literature and with original contributions by the author.

The material presented here should serve as an excellent refresher course in Obstetrics and Gynecology.

RUSSELL R. DE ALVAREZ

²⁴**Caring for the Premature Baby.** By Lillian Saltzman, R.N. 139 pages with 6 illustrations. Boston, 1951, Chapman & Grimes. \$2.50.

²⁵**Atlas der Pathologischen Anatomie (Eine Sammlung typischer Krankheitsbilder der menschlichen Organe).** By Prof. R. Rössle, formerly Professor of Pathology and Director of the Pathological Institute of Berlin at Charité-Krankenhaus, and Dr. K. Apitz, Prosector of Charité-Krankenhaus. 298 pages with 564 illustrations, mostly colored. Stuttgart, 1951, Georg Thieme. 87 DM.

²⁶**Primer Congreso Mexicano de Ginecología y Obstetricia.** By La Asociación Mexicana de Ginecología y Obstetricia y Sociedades Filiales. May 22-28, 1949, Mexico.

Items

The Fifth American Congress on Obstetrics and Gynecology

Netherland-Plaza Hotel, Cincinnati, Ohio

March 31 through April 4, 1952

Program

Monday Morning

9:00 Registration

10:30 Invocation

Welcome by President of Cincinnati Academy of Medicine

Welcome by President of Cincinnati Obstetrical-Gynecological Society

Welcome by President of Ohio State Medical Association

Address by President of American Committee on Maternal Welfare

Address by General Chairman of American Committee on Maternal Welfare

Address by Program Chairman of American Committee on Maternal Welfare

Monday Afternoon

1:30 Two Concurrent Meetings

A. CHICAGO'S 10,000 NEONATAL AUTOPSIES

Autopsy Procedure—Edith M. Potter, M.D., Chicago

Methods of Assembling and Tabulating Pathological Reports—Mr. Frank Bauer, Chicago

Epidemiologic Approach and Analyses—William Fishbein, M.D., Chicago

Positive Actions Taken—Herman N. Bundesen, M.D., Chicago

B. STERILITY

Chairman: Isador C. Rubin, M.D., New York

Minimum Standards for Sterility Investigations—John O. Haman, M.D., San Francisco

Discussion—Leo J. Hartnett, M.D., St. Louis

Role of Surgery—Charles E. Galloway, M.D., Evanston, Ill.

Discussion—Robert N. Rutherford, M.D., Seattle

Endocrine Therapy—Somers H. Sturgis, M.D., Boston

Discussion—Laman A. Gray, M.D., Louisville

3:45 Concurrent Panel Discussions

A. COMPLICATIONS OF PUERPERIUM

Moderator: Conrad G. Collins, M.D., New Orleans

Panel Participants: Seward H. Wills, M.D., Houston

Herbert E. Bowles, Honolulu

Edward G. Waters, M.D., Jersey City, N. J.

More Panel Participants:

Hugh G. Hamilton, M.D., Kansas City, Mo.

Donald G. Tollefson, M.D., Los Angeles

Willis E. Brown, M.D., Little Rock

B. RH AND HR SENSITIZATION

Moderator: Jean Paul Pratt, M.D., Detroit

Panel Participants:

Present Day Concepts of Rh and Hr Sensitization—Philip Levine, M.D., Raritan, N. J.

Experience With ACTH in Sensitized Patients—Emil G. Holmstrom, M.D., Salt Lake City

Exchange Transfusions—Louis K. Diamond, M.D., Boston

Tuesday Morning

9:00 Two Concurrent Meetings

A. PRENATAL CARE ACROSS AMERICA

Chairman: Herman N. Bundesen, M.D., Chicago

Maternal Care in a Large Metropolitan Area—Helen M. Wallace, M.D.,
New York City

Maternal Care in a Rural Area—D. V. Galloway, M.D., Jackson, Miss.

Maternal Care in a Mountain Area—R. L. Cleere, M.D., M.P.H. Denver

B. SYMPOSIUM ON DYSTOCIA

Chairman: William F. Mengert, M.D., Dallas

Prolonged Labor—J. P. Greenhill, M.D., Chicago

Discussion—W. N. Thornton, Jr., Charlottesville, Va.

Pelvic Contraction—D. Frank Kaltreider, M.D., Baltimore

Discussion—Howard C. Moloy, M.D., New York

Breech Presentation—Gerald W. Gustafson, M.D., Indianapolis

Discussion—Emmett D. Colvin, M.D., Atlanta

Indications for Cesarean Section in Dystocia—R. Gordon Douglas, M.D.,
New York City

Discussion—J. Randolph Perdue, M.D., Miami, Fla.

11:00 Panel Discussion

A. ORGANIZATION AND OPERATION OF GOOD MATERNAL MORTALITY COMMITTEES

Moderator: Philip F. Williams, M.D., Philadelphia

Panel Participants: (Some to be announced.)

Hospital Level—

City or County—James M. Alesbury, M.D., Philadelphia

State—

Federal—

Tuesday Afternoon

1:30 Two Concurrent Meetings

A. MATERNITY CARE TODAY—WHAT IS NEEDED FOR TOMORROW?

Chairman: Miss Ruth Taylor, R.N., Washington, D. C.

Panel Participants: Betsy Wooten, M.D., Baltimore

Samuel Wishik, M.D., Pittsburgh

Hazel Corbin, R.N., New York City

B. URINARY INCONTINENCE

Chairman: John W. Huffman, M.D., Chicago

Incontinence Due to Local Lesions in Urethra and Bladder—Houston E.
Everett, M.D., Baltimore

Marshall-Marchetti Procedure for Stress Incontinence—Andrew A. Marchetti,
M.D., Washington, D. C.

Kelly and Sling Operations for Incontinence—Albert H. Aldridge, M.D.,
New York City

Vesicovaginal Fistula—Experience at the Mayo Clinic—Virgil S. Counseller,
M.D., Rochester, Minn.

3:45 Concurrent Panel Discussions

A. MATERNAL MORTALITY

Moderator: J. Robert Willson, M.D., Philadelphia

Panel Participants:

C. Hampton Mauzy, Jr., M.D., Winston-Salem, N. C.

Charles Newberger, M.D., Springfield, Ill.

Paula M. Horn, M.D., Los Angeles

John H. Moore, M.D., Grand Forks, N. D.

Deborah Leary, M.D., New Haven, Conn.

B. LESIONS OF THE VULVA

Moderator: Robert J. Crossen, M.D., St. Louis

Panel Participants:

Carcinoma—Walter L. Thomas, M.D., Durham, N. C.

Granuloma, Lymphogranuloma and Chancroidal Diseases—Robert B. Greenblatt, M.D., Augusta, Ga.

Luetic Lesions—Charles S. Stevenson, M.D., Detroit

Systemic and Allergic Diseases of the Vulva—John Parks, M.D., Washington, D. C.

C. PREPARATION FOR CHILDBEARING

Speakers: To be announced.

*Wednesday Morning***9:00 Concurrent Meetings****A. DOCTOR, NURSE, PARENTS—CAN THIS TEAM WORK TOGETHER?**

Speakers: To be announced.

B. SYMPOSIUM ON UTERINE CARCINOMA

Chairman: James A. Corscaden, M.D., New York City

Diagnostic Studies—Joe Vincent Meigs, M.D., Boston

Discussion—W. G. Cosbie, M.D., Toronto, Canada

Treatment of Cancer of the Cervix—Herbert E. Schmitz, M.D., Chicago

Discussion—Axel N. Arneson, M.D., St. Louis

Treatment of Cancer of the Endometrium—John L. McKelvey, M.D., Minneapolis

Discussion—Lewis C. Scheffey, M.D., Philadelphia

Place of Extensive Pelvic Surgery—F. Bayard Carter, M.D., Durham, N. C.

Discussion—Daniel J. Morton, M.D., Los Angeles

11:00 WHAT CAN BE LEARNED—FROM THE WORLD HEALTH ORGANIZATION? FROM PARENTS? OBSTETRICIAN? NURSE?

Speakers: To be announced.

*Wednesday Afternoon***1:30 Two Concurrent Meetings****A. OBSTETRIC HEMORRHAGE**

Chairman: Samuel A. Cosgrove, M.D., Jersey City, N. J.

Hemorrhage in First and Second Trimesters—C. O. McCormick, Sr., M.D., Indianapolis

Discussion—Albert W. Diddle, M.D., Knoxville, Tenn.

Abruptio Placentae and Placenta Previa—M. Edward Davis, M.D., Chicago

Discussion—Douglas M. Cannell, M.D., Toronto, Canada

Prevention and Treatment of Postpartum Hemorrhage—Raymond A. Schwegler, Jr., M.D., Lawrence, Kan.

Discussion—Roland S. Cron, M.D., Milwaukee

B. ARE FUNDAMENTAL ADMINISTRATIVE CHANGES NECESSARY TO THE PROVISION OF TOMORROW'S MATERNITY CARE?

Chairman: Miss Gertrude Church, R.N., San Francisco

First Panel: Hilda Kroeger, M.D., Pittsburgh

Thelma Ryan, R.N., New York City

Kate Hyder, R.N., New York City

Second Panel: Elizabeth Peck, R.N., Syracuse, N. Y.

Lottie Morrison, R.N., New York City

Mary Edna Fitzpatrick, R.N., Atlanta

3:45 Concurrent Panel Discussions**A. ENDOMETRIOSIS**

Moderator: Richard W. Te Linde, M.D., Baltimore

Panel Participants: Roger B. Scott, M.D., Cleveland
Edwin Robertson, M.D., Kingston, Ont., Can.
George H. Gardner, M.D., Chicago
Willard R. Cooke, M.D., Galveston
Joseph W. Kelso, M.D., Oklahoma City

B. PREGNANCY COMPLICATING MEDICAL CONDITIONS

Moderator: John W. Harris, M.D., Madison, Wis.

Panel Participants:

Tuberculosis and Pregnancy—Lawrence M. Randall, M.D., Rochester, Minn.
Heart Disease and Pregnancy—Russell J. Moe, M.D., Duluth
Steroid Hormones as an Adjunct in the Management of Pregnancy Complicating Diabetes—Priscilla White, M.D., Boston
Management of the Diabetic Pregnant Patient—Ralph A. Reis, M.D., Chicago

7:30 BANQUET (Dress Optional)

Thursday Morning

9:00 SOCIAL ASPECTS OF MATERNAL CARE

Chairman: William Benbow Thompson, M.D., Los Angeles, Cal.

Proposed E.M.I.C. Legislation—Joseph Lawrence, M.D., Washington, D. C.
How Can the Obstetrician Help the Public Health Officer?—Buford Hamilton, M.D., Missouri
How the Obstetrician Can Influence Public Relations—Mr. Leo E. Brown, Chicago, Director of Public Relations, American Medical Assn.

11:00 EDUCATIONAL ASPECTS OF MATERNAL CARE

Chairman: William Benbow Thompson, M.D., Hollywood, Cal.

The Education of the Patient—Milton G. Potter, M.D., Buffalo, N. Y.
The Vertical Teaching Program—Frank Lock, M.D., Winston-Salem, N. C.
Post-Graduate Midwinter Assemblies—George Judd, M.D., Los Angeles, Cal.
The Education of the Hospital—Edwin M. Gold, M.D., New York City

Thursday Afternoon

1:30 Two Concurrent Meetings

A. OVARIAN TUMORS

Chairman: Robert L. Faulkner, M.D., Cleveland

Benign Tumors—Curtis J. Lund, M.D., New Orleans
Discussion—Allan C. Barnes, M.D., Columbus, Ohio
Malignant Tumors—Howard C. Taylor, M.D., New York City
Discussion—Kenneth T. MacFarlane, M.D., Montreal, Can.
Hormonally Active Tumors—Emil Novak, M.D., Baltimore
Discussion—John C. Burch, M.D., Nashville

B. TOXEMIAS

Chairman: Edward L. King, M.D., New Orleans

Etiology of Toxemias—William J. Dieckmann, M.D., Chicago
Discussion—Frank E. Whitacre, M.D., Memphis, Tenn.
Treatment of Toxemias—Russell R. Dealvarez, M.D., Seattle
Discussion—Rudolph A. Bartholomew, M.D., Atlanta, Ga.
Treatment of Toxemias—Stanley T. Garber, M.D., Cincinnati
Discussion—Lester D. Odell, M.D., Omaha, Neb.

3:45 Concurrent Panel Discussions

A. UTERINE BLEEDINGS

Moderator: Robert A. Kimbrough, M.D., Philadelphia

Panel Participants:

Functional Bleeding—Willard M. Allen, M.D., St. Louis
Myomas of the Uterus—W. Nicholson Jones, M.D., Birmingham, Ala.

More Panel Participants:

Hydatidiform Mole and Chorionepithelioma—Albert W. Holman, M.D., Portland, Ore.

B. CESAREAN SECTION

Moderator: Edward A. Schumann, M.D., Philadelphia

Panel Participants:

Indications for Cesarean Section—Herman W. Johnson, M.D., Houston, Texas
Analgesia and Anesthesia—T. L. Montgomery, M.D., Philadelphia
Evaluation of Operative Techniques—H. Hudnall Ware, M.D., Richmond, Va.
Obstetric Future of the Cesareanized Patient—Robert A. Cosgrove, M.D., Jersey City, N. J.

Friday Morning

9:00 General Meeting

FETAL WASTAGE

Role of Endometrium in Implantation and Fetal Growth—Edward C. Hughes, M.D., Syracuse, N. Y.

Discussion—Arthur T. Hertig, M.D., Boston

Pathology of Perinatal Death—George W. Anderson, M.D., Baltimore, Md.

Discussion—D. Anthony D'Esopo, M.D., New York City

Safeguarding the Newborn—The Obstetrician's Responsibility—E. Stewart Taylor, M.D., Denver

Discussion—William C. Keettel, M.D., Iowa City, Iowa

Safeguarding the Newborn—The Pediatrician's Responsibility—Clement A. Smith, M.D., Boston

Discussion—Alexander A. Weech, M.D., Cincinnati

Fellowship in Obstetric and Gynecologic Endocrinology

The next Fellowship in Obstetric and Gynecologic Endocrinology in the Jefferson Medical College and Hospital will be available, July 1, 1952. At least one year of preliminary training in obstetrics and gynecology or in endocrinology is required. Requests for application should be sent promptly to Dr. Lewis C. Scheffey, Chairman of the Department of Obstetrics and Gynecology, Jefferson Medical College.

A. E. RAKOFF, M.D.

Clinical Professor of Obstetric
and Gynecologic Endocrinology

Thirteenth British Congress of Obstetrics and Gynaecology

The Thirteenth British Congress will be held in Leeds, England, July 8 to 11, 1952.

Among the guest speakers will be Dr. Albert H. Aldridge, Director of the Woman's Hospital, whose topic is "Stress Incontinence of Urine."

For further information apply to Brian Jeaffreson, F.R.C.O.G., Hon. Secretary, The Hospital for Women, Coventry Place, Leeds, England.

German Gynecological Society

The Twenty-ninth Meeting will be held in Munich, Germany, Oct. 7-11, 1952. As numerous foreign contributors, including American, will be on the program, this gathering has assumed an international character.

